DIPHTHERIA

AND ITS

ASSOCIATES

LENNOX BROWNE

Every increase of knowledge brings before us a larger and clearer view of the immeasurable quantity which is still to be gained. The more we know, the more can we see, if we will, how much more there is that we do not know.

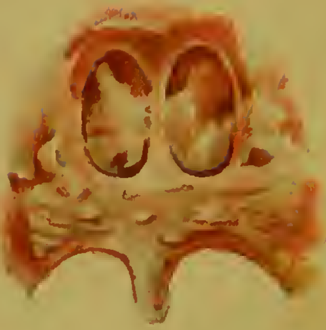
. . . .

Where are we to stop? I do not know more than this: that we must not stop where we are; we must go on and on, and we may be sure that they who work to find the truth will not work in vain.

SIR JAMES PAGET,
Presidential Address to the Pathological Society of London,
1887.

DIPHTHERIA.

Faucial aspect.



Post nasal aspect.

Laryngoscopic appearance.

Post mortem appearance.

Lennox Browne ad natm del.

DIPHTHERIA

AND ITS ASSOCIATES.

BY

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PREFACE.

The subject of Diphtheria has been one of deep interest to me since the days of my pupilage, and has occupied active attention in each of the four editions of my systematic work on Diseases of the Throat as they have appeared at intervals since 1878.

The present essay is based mainly on a course of lectures recently delivered, for the purpose of establishing a landmark at an important era in the history of diphtheria, and of emphasising the desirability of assimilating the teachings of bacteriology to the purposes of practical medicine. In other words, to indicate the necessity for the scientific expert and the clinician to work together as colleagues, and not as rivals.

It must be thankfully conceded that clinical observations frequently gain additional confirmation, not infrequently a new significance, and even in a few instances correction, when examined by the light of bacteriological science.

On the other hand, it is suggested that an undue tendency has arisen to evolve all the essential clements of diphtheria and of some other diseases—etiology, diagnosis, pathology, prognosis, and even treatment—from material afforded by animal experiments, the culture tube, microscope, and retort, and to ignore the value of bedside evidence, however authoritatively expounded, and however long held as an article of faith, whenever it cannot be brought into exact harmony with the latest bacteriological utterance.

But the value of all facts acquired in the laboratory must of necessity depend on their ability to stand the crucial test of bedside application; because, whatever the source of information, the saving of human life should always constitute the paramount object of all professors of the healing art. Whether I have been successful in laying down correctly the lines of a safe middle course, the following pages must testify; that, at any rate, is the aim of this attempt.

Every endeavour has been made to give the latest views on each separate branch of this vast subject, and for this purpose the opinions of recognised authorities are largely quoted. It is not, however, for a moment suggested that this essay is to be accepted as in any degree exhaustive. With the mass of literature and information at command, that were a task almost sufficient for a lifetime.

It is a pleasurable duty to thankfully acknowledge the opportunities afforded by the Metropolitan Asylums' Board to follow the course of Diphtheria, as exhibited and treated according to modern views, in one of their hospitals, in a manner and to an extent that is impossible for one who, in consulting practice, but too often sees a case when the malady is so far advanced that the patient is practically beyond hope of recovery.

To Dr. Gayton, Superintendent of the North-Western Fever Hospital, whose wards I have attended, I owe an especial debt of gratitude for the great liberality with which he has permitted me to acquire information, for his zeal and co-operation in my work, and for much wise counsel, the outcome of a unique experience, which cannot fail to give value to a large portion of what I have to say.

To the Clinical Research Association I am indebted for the

great trouble taken with the bacteriological examination of the cultures I have made, and for the excellent microscopic slides which have enabled me to secure such characteristic photo-micrographs. These have been obtained at great pains, but with fully compensatory results, by Mr. Lees Curtis, of Messrs. Baker & Co., under my personal supervision, with the more than capable aid of my assistant, Dr. Holloway, who is an expert with microscope, camera, and lantern. The photo-micrographs have been "processed" with great exactitude by Mr. Carl Hentschel, and my own drawings have been very faithfully rendered by Messrs. Scott & Ferguson of Edinburgh, to whom my thanks are also due for the careful printing of a book requiring so many diverse qualifications for the successful achievement of its production.

15 Mansfield Street, W.,
June 1895.

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AND ITS ASSOCIATES.

Diphtheria and its Associates.

DEFINITION AND SYNOPSIS.

Diphtheria is an acute infectious disease due to the presence of a specific micro-organism (the Klebs-Loeffler bacillus).

1. Diphtheria is to be considered as **simple** or **pure** when this specific bacillus constitutes the *sole* organism; and it may then be termed **simple bacillary** diphtheria.

2. Diphtheria is to be considered *complex* or *impure* when the bacillus is *associated* with other micro-organisms, which are chiefly cocci, and may, in these circumstances, be termed **complex** or **cocco-bacillary** diphtheria.

3. The term *pseudo* or *false diphtheria* represents an affection of the throat resembling diphtheria, but distinguished from either the simple or complex varieties by the *conspicuous absence* of the *specific bacillus.* It may thus be termed **non-bacillary** diphtheria.

4. The term *pseudo-diphtheria* has also been erroneously applied to an affection of the throat characterised by the presence of a bacillus *identical* with the Klebs-Loeffler in every respect *save that of virulence.* A preferable term would be **non-virulent bacillary** diphtheria.

To avoid confusion, the terms "diphtheria," "diphtherial," and "diphtheric" will alone be employed in this Essay to designate the phenomena caused by the presence of the Klebs-Loeffler

bacillus, whether present alone or in association with other micro-organisms.

The morbid influence of diphtheria due to its microbic origin is manifested in three distinct directions, two of which are common to both the simple and the complex forms; the third is an additional characteristic of the complex variety, and is the sole bacterial expression of non-bacillary diphtheria.

First. The **Inflammatory process,** which is accompanied by an exudation of false membrane; this is almost invariably first deposited on the *tonsils* and *fauces,* which may constitute its sole site, but the exudation may extend upwards to the *nares*; to the *middle,* or even the *internal ear,* by the Eustachian tubes, or downwards to the *larynx* and *trachea,* as far even as the minute *bronchi.* The specific membranous inflammation may, as a quite rare exception, *commence* in the *nares* or *larynx;* equally seldom is it limited to either situation; and still less often does it extend to the *œsophagus* or *stomach.* Diphtheria occasionally attacks the *conjunctiva,* as well as *wounds* of the *skin* and *abrasions* of the *mucous membranes* of other parts than those already named. As a result of this inflammatory process in the throat, **death** may occur from **mechanical obstruction** of the air passages.

Secondly. The poisonous qualities and products of the bacillus cause **systemic intoxication,** which is manifested, first by rapid death due to *paralysis* of *vital functions,* and as a later manifestation, in those who survive, by *degenerative changes in the nerves and muscles.*

Thirdly. The presence of associated organisms, especially streptococci and staphylococci, is responsible for the occurrence of the characteristic **phlegmonous** and **pyæmic** processes.

Finally. Pseudo, false, or non-bacillary diphtheria is distinguished by the *absence* of the specific **toxæmia,** though both the **inflammatory** and **pyæmic** processes may be exhibited in equal intensity with those of the true disease.

CHAPTER I.

HISTORY.

750 B.C. to A.D. 1884.

The earlier accounts of diphtheria are of necessity confused, in that all the various forms of throat inflammation, characterised by the presence of false membranes, as well as others that were not, are included under the common but inexpressive terms of "Cynanche" and "Angina," and no purpose would be served by giving any detailed account of the views of earlier writers, or in attempting to harmonise their descriptions of diphtheria with our present knowledge. Suffice it to say that, from so far back as seven or eight hundred years before the Christian era, authors, whose number is legion, of every nationality, from D'Hanvantare—an Indian physician, contemporary with Pythagoras—onwards, have described, under various names, an affection of the throat, which can be interpreted to bear a more or less complete resemblance to diphtheria as we at the present time recognise it.

Those who are interested in pursuing their studies in the bibliography of diphtheria may be referred to the writings of Bretonneau (1823-1855), of Deslandes (1827), Fuchs (1828), Headlam Greenhow (1860), Jacobi (1877), Rauchfuss (1878), Morell Mackenzie (1879), and Ruault (1892), each of whom has contributed interesting and curious historical details with a completeness which it would be difficult to emulate and impossible to excel.

The following are a few of those whose writings stand out as in any degree original or of prominent merit :—

ASCLEPIADES (100 B.C.). The first to recommend laryngotomy.

ARETÆUS, flourishing in the second half of the first century, gave descriptions of the objective appearances of the disease, which would almost apply to it at the present day.

AETIUS, of Mesopotamia, in the sixth century, pointed out the danger of tearing away the false membrane; and then, after a long interval, comes—

BAILLOU, who, in 1576, recorded the occurrence of an orthopnœic affection of the throat, undoubtedly diphtheria, though considered by Bretonneau to be descriptive rather of false croup—otherwise non-diphtherial laryngitis.

Passing over numerous contributions from Italy, Spain, Sweden, and Holland in the sixteenth and seventeenth centuries, and an excellent account of an epidemic in Cornwall, by STARR, in 1750, we come to the work of FRANCIS HOME, a Scotch physician, who in 1765 gave, under the names of "suffocatio stridula" and "catarrhus suffocativis," what may fairly be called a classical account of croup, as it was then named, and as it is still termed by the French when the larynx and trachea are involved.

Some practical monographs were written in America by BARD in 1789, and ARCHER in 1798, and we learn from Bretonneau and Morell Mackenzie, that it was from croup—the French synonym for laryngo-tracheal diphtheria—that the great George Washington died in 1799, though his death is ascribed by most lay biographers to laryngitis, supervening on exposure to a severe snow storm whilst riding round his farms.

In 1807 the nephew of the first Napoleon died from diphtheria at the Hague, within a few weeks of his father Louis, the brother of Napoleon, being invested as King of Holland. As a result of these disasters the Emperor offered a substantial prize for the essay which should give the fullest information "how best to arrest the progress of croup and its inroads." Other relatives of Buonaparte, amongst them the unhappy Empress Josephine and her grandchild, were later attacked, and succumbed.

We learn that no less than eighty-three memoirs were sent in

for adjudication, and that the prize was divided between two of the competitors—JURINE of Geneva, and ALBERS of Bremen.

Nothing could more forcibly demonstrate the great lack of information which then generally obtained as to the disease than a consideration of the opinions and the methods of treatment enunciated by these authors, but to quote from their writings would be only "to thrice slay the slain."

It was reserved for BRETONNEAU of Tours,—in his famous work, entitled "*Des inflammations spéciales du tissu muqueux*," which, written in 1821, was not published till 1826,—to give a complete account of the disease as it had been exhibited during a terrible epidemic in the city in which he practised. This was followed by subsequent valuable memoirs on the same subject extending to the year 1855.

Among the points of interest particularly brought out by this observer, was the minor position that diphtheria takes with regard both to contagion and gangrenous ulceration, as compared with scarlet fever and other diseases of this class, and his recognition of the systemic poisoning so characteristic of diphtheria, as evidenced by the occurrence of paralysis. He also drew attention to nasal diphtheria, to epidemic influenza as a predisposing cause, and to many other clinical features, not a few of which are brought under our notice from time to time as novelties.

The vigour with which Bretonneau pursued his local applications of nitrate of silver—a mode of treatment first recommended by MACKENZIE of Glasgow in 1825—was probably responsible for the long delayed recognition of the essential importance of topical remedial measures in the scientific treatment of this disease. Bretonneau was also the first to administer mercury for this malady, which he did both by calomel given internally, and by inunctions with mercurial ointment. Not the least interesting and instructive of his experiences are the careful records of numerous necropsies which were performed under his personal supervision.

Bretonneau's observations were generally confirmed by those of GUERSANT (1835), who took special trouble to rescue the

nosography of diphtheria from the confusion into which it had fallen.

TROUSSEAU directed his exceptional powers of clinical observation to establishing a differential diagnosis between true and false diphtheria, especially that variety due to scarlet fever. His lectures on this subject have more than the usual charm of style which characterise his writings, since their delivery was largely prompted by the loss of more than one colleague and dear friend from the malady.

Trousseau was one of the first to point out that the danger of this disease is manifested in two directions—first, by extension of the membrane to the air passages, and secondly, in an ataxo-adynamic form, in which the patient is carried off without any such extension. He may also be said to have greatly assisted Bretonneau in establishing the operation of tracheotomy as the justifiable and even hopeful *dernier ressort* of diphtheria, and in gaining for it increased acceptance; his indications for its adoption and the details of its performance giving us accurate data for guidance up to the present day.

BOUCHUT merits especial mention as a man of exceptional genius and ability, and as one who was indeed considerably in advance of his time; for he it was who first practiced *tubage*,* a procedure so condemned at that period as to fall into disuse for nearly a quarter of a century, until its successful revival and perfection as intubation in 1880 by O'DWYER and other American physicians.

Bouchut, recognising the primarily local nature of the disease, was also the first to remove hypertrophied tonsils during the acute stage of diphtheria, for the special purpose of preventing the downward extension of the membrane to the air passages. He recorded four cases of successful operation, in none of which did the deposit re-form on the wounded surfaces.

DAVIOT adopted the same measures, and recorded a case. He was also an advocate for forcible removal of the membrane, giving

* Morell Mackenzie ascribes priority to Loiseau (Bullet. de l'Acad. de Méd., 1857).

it as his opinion "that the effects of cauterisation are never more certain than when we are operating on the surfaces denuded of their pseudo-membranes."

Notice was directed to the frequency and importance of albuminuria in relation to diphtheria by WADE, BOUCHUT, and EMPIS, in 1858; their labours appearing to have been almost synchronous and independent.

Of other writers of note in the middle of the present century we may name VIRCHOW, who in 1847—in his special domain of pathological research—described, with his usual accuracy, the morbid anatomy of the parts affected by diphtheria as at that time recognised.

In 1854, VON GRAEFE was the first to note diphtheric conjunctivitis, and WEST in this country alluded to diphtheria as following measles, though at that time he had seen but little of it as a primary disease.

We find subsequently the honoured names of several English physicians as authors of many more or less scattered contributions to the literature of this subject, of whom thereof WATSON, GULL, WILKS, HARLEY, LIONEL BEALE, and BURDON SAUNDERSON, may be mentioned.

The great epidemic in England, which commenced in 1855, was believed to have been imported from Boulogne *viâ* Folkestone. It raged almost without intermission until 1860, and it was only on its termination that English medical literature became enriched by contributions worthy of the theme. It is sufficient to name the statesmanlike reports to the Privy Council of Mr. (afterwards Sir John) SIMON, and the volumes of HEADLAM GREENHOW, HILLIER, and, last but by no means least, Sir WILLIAM JENNER, whose clinical lectures on diphtheria, published in 1861, are richly endowed with the keenness of perception, as well as the terseness and directness of utterance, which form the distinguishing features of all that has come from the pen of this eminent and revered teacher.

Jenner originally believed that diphtheria—especially so far

as the throat manifestations are concerned—is altogether a different disease from scarlet fever, of which it was supposed to be a modification. Admitting, however, the probability that the two diseases are closely allied, he also wrote as follows:—"Are diphtheria and croup essentially the same disease? I think not, because there is no evidence to show that croup is anything more than a local disease, that it is contagious, that it occurs as a wide-spread epidemic, that it affects a large proportion of adults, that there is albumen in the urine, that symptoms of disordered innervation follow recovery from the primary affection. We must not confound diphtheritic exudations with diphtheria."

It was in the spring of 1878 that I had published the first edition of my systematic work, in which I declared myself a non-identitist, and I have continued to do so in all the various editions that have since appeared, because of the teachings received in the early days of my pupilage, in 1858, spent in a district where the great English outbreak was notably accentuated.

My principal, the late Mr. BROOKS of Henley-on-Thames, never lost an opportunity of impressing on me that there was an old disease known as croup, which was capable of being distinguished from a new one called diphtheria, and of insisting on the diagnostic differences and characteristics of the two. Those early impressions were never effaced, nor did my interest in diphtheria ever wane; while, with increased opportunities of clinical observation, I became more than ever impressed with the truth of my early instruction—that is to say, I was never able to bring myself to admit that every acute membranous inflammation of the throat and larynx is a true diphtheria; and, by a logical inference that every case requires the same treatment. I can particularly recall the pride I had felt that Sir William Jenner held the same view, and the feeling almost akin to shock which I experienced when, in 1875, he changed his opinion, and was quoted as giving his adhesion to the views of a Committee of the Royal Medico-Chirurgical Society, especially appointed "to investigate the relations between membranous croup and diphtheria."

In 1878 this body collected a mass of highly interesting matter, embracing hospital statistics and the private records and opinions of general physicians and practitioners. The main conclusions arrived at by the Committee were in favour of considering laryngo-tracheal diphtheria and membranous laryngitis as identical, though careful perusal of the whole document brings out very strongly the fact that a large majority of those who contributed to the investigation by answering the Committee's circular of questions were so clear in their opinion that non-specific membranous laryngitis exists (and is met with in practice) as an entirely distinct disease from primary laryngo-tracheal diphtheria, that it was impossible for the Committee to speak more definitely.

I feel constrained to add that some of the Committee's conclusions, notably those regarding the influence of cold *per se* to produce croup, and on the question of contagion, appear to be in direct contradiction of the evidence which they published. The late Sir GEORGE BURROWS, Professor LAYCOCK, and Dr. WILKS, may be particularly named amongst those who gave testimony opposed to the report.

Just about this time, the latter end of 1878, occurred the lamented death, from diphtheria, of the PRINCESS ALICE, Grand Duchess of Hesse, a beloved and highly gifted daughter of our Sovereign. The disease was contracted shortly after nursing the Grand Duke and five of her children during an outbreak of the same malady, to which one—the Princess Marie—succumbed. Immediately afterwards, Sir MORELL MACKENZIE published his scholarly monograph on diphtheria, a chapter in advance of his classical "Manual on Diseases of the Throat." The essay is a type of all that issued from Mackenzie in respect of fulness of detail, wealth and accuracy of reference, and grace of language, but unfortunately he gave unqualified assent to the diphtherial identity of all forms of membranous laryngitis, as did several other distinguished authors of systems and dictionaries of general medicine, though exceptions must be

credited to such eminent authorities as Sir WILLIAM AITKEN, TANNER, BROADBENT, F. ROBERTS, and HILTON FAGGE.

And so matters continued until 1884, a year made memorable by the discovery, or rather by the recognition and acceptance, of a specific organism of the disease, namely, the KLEBS-LOEFFLER bacillus. This circumstance settled not only the question in favour of the non-identity of all forms of membranous inflammations of the upper air passages, but also that of the local origin of diphtheria. The events which led to this epoch-making circumstance, as well as to its further development, must be reserved.

CHAPTER II.

ETIOLOGY.

CLIMATE—SOIL—SANITATION—PRECEDING OR CONCURRENT EPIDEMICS —CONSTITUTIONAL STATES—MODES OF DISSEMINATION.

Logically, the etiology of diphtheria might be comprised in a description of its specific organism, with its local manifestations and its systemic effects, and such has been the course pursued by those who are commonly described as scientists; but important as it is that every detail in the life history of the bacillus, its congeners and associates, as well as their varieties, from the double point of view of culture ground and virulence, should be duly estimated, those who have to battle with the disease at the bedside, and also to prevent its extension, must go still further back, and seek for some measure of exactitude in first causes, as compared with those accepted in relation to the etiology of other specific diseases of zymotic origin.

It has to be remembered that diphtheria may arise either epidemically, endemically, or sporadically. There can be little doubt, however, that receptivity to infection depends largely on some ill-defined though fairly well understood insanitary circumstance of region, atmosphere, or individual; and accepting this as our view, we shall proceed to discuss :—

First. The predisposing causes of the origin of diphtheria, and some of the obvious agents by which the disease can be disseminated.

Secondly. The diphtherial entity, in other words, the specific organism, its toxic products and effects, and other organisms which may be associated with it.

Testimony on the first division of our subject is as profuse as it is contradictory, being largely anecdotal and irresponsible. It has therefore appeared advisable to take, as the most reliable evidence, the reports which have been made (45 in number) to the Local Government Board by various deputed inspectors, partly because the witnesses are experts, partly also because the reports have all been submitted to the revision of distinguished chiefs before publication, but mainly because there is a certain uniformity of method in their construction. They embrace particulars of all important outbreaks for the last twelve years, the first bearing date 26th December 1882, and the last 27th November 1894.

The tabular abstract of these reports appended to this section will show at a glance the main features on which they are based, and brief comments will be given under each heading; but before considering those of domestic and rather individual interest, a few words are necessary as to broader features which may influence the causation of prevalences.

The Predisposing Causes.

These require to be further subdivided into :—

(*a*) Climatic and domestic surroundings.

(*b*) Preceding or concurrent epidemics of other specific fevers, as well as the development of a pseudo-diphtheria into an attack of the true disease.

(*c*) Constitutional predisposition.

The Influence of Climate.

Under this comprehensive heading may be included geographical distribution, geological conditions, the amount of the rainfall, and the influence of season.

Geographical.—Dr. Thursfield was the first to demonstrate that the mortality from diphtheria is nearly three times greater in rural districts than in urban. He has also remarked that those conditions of soil which tend to promote fungoid growths, appear to

favour the incidence and persistence of the disease. Dr. Longstaff, following the same line, has made some careful and valuable reports on the geographical distribution of diphtheria. Dividing England and Wales into eleven registration districts, he makes his comparison (1) in regard to the mean annual death-rate from diphtheria, (2) in regard to the density of population, and (3) in regard to the mean annual death-rate from all causes, which is taken for England and Wales as 100, so that the excess of each division is read off in percentages of the mean.

Lastly, he divides the 26 years (1855-1880) included in his report into three different periods.

The important question in relation to our present subject is that of the density of the population, and for the purposes of classification the districts are further subdivided into—

(1) **Dense districts.**—Those in which there is less than one acre of surface to each person.

(2) **Medium districts**, in which there is more than one acre, but less than two acres.

(3) **Sparse districts**, in which there is more than two acres to each inhabitant.

These investigations show that density of population cannot be considered as an important factor in the production of fatal diphtheria; on the contrary, the malady is proved to be more fatal in the rural and sparsely populated districts, thus fully supporting Dr. Thursfield's earlier conclusions.

It has been further demonstrated that "the geographical distribution of other zymotic diseases is totally different from that of diphtheria. That summer diarrhœa is especially a disease of towns is a familiar fact to which attention has repeatedly been called by the Registrar-General. Measles is especially fatal in London. Scarlet fever is most common in the mining and manufacturing counties," while diphtheria is manifested in these same manufacturing districts in very varying degrees of intensity.

This fact still obtains, but it has undergone some degree of modification. Thus, in the first period, the relative mortality of

diphtheria in the different districts proves the malady to have been twice as fatal in sparse and rural areas as in large towns, while districts with medium density of population occupied a middle position. In the second period the results were less striking, and in the third the differences were still less marked.

Assuming the mortality of the dense districts as 100, and striking an average of the three periods, the result gives—

Mortality in dense districts,	. . .	100
„ medium „	. . .	118
„ sparse „	. . .	151

A map accompanies Dr. Longstaff's interesting reports, in which the counties are tinted, so that the depth of colour is proportional to the mortality; and this emphasises the circumstance that diphtheria has a strong predilection for scattered rural populations, and even for districts reputed to be exceptionally healthy as regards other infectious diseases.

In each succeeding decade, however, the urban districts have been found to suffer more and more relatively to the rural.

Two questions may therefore be asked—

1. What are the predisposing causes which account for a greater frequency of diphtheria in sparsely populated districts?

2. To what may we attribute the gradual increase of an urban prevalence which has led to the greater approach to equal mortality with that in sparse districts?

The first question may be further divided with regard to two other factors, (*a*) those of origin, and (*b*) those of dissemination.

(*a*) As to **origin**—

Amongst other causes which may be sought for, primitive modes of life, the development of vegetable organisms in damp dwellings, defective and polluted water supplies, and lastly, frequent and close relation with animals in the farm yard—cows, pigs, fowls, &c., have all been given a certain weight, and a close etiological relationship has been claimed between outbreaks of diphtheria in the human subject and epidemics of certain diseases

of animals, such as pleuro-pneumonia and foot and mouth disease, as well as with "diphtheria in fowls, pigeons, and cats."

Notwithstanding that we somewhat anticipate the question of the diphtherial entity, this appears an appropriate place to consider briefly the so-called diphtheria of animals in relation to human infection.

Loeffler, for instance, in 1884 described a diphtheria of calves due to the "bacillus diphtheriæ vitulorum," but neither in its morphological or biological characters, nor in its pathogenesis, is their much similarity between this organism and that of diphtheria in the human subject.

Much the same may be said as to the diphtheria or tuberculo-diphtheria of fowls and pigeons. There is no evidence to show that this disease is capable of conveying diphtheria to man, and Professor Nocard, the well-known veterinary surgeon attached to the Pasteur Institute, most positively affirms that human diphtheria is entirely separate and distinct from that of fowls.

Nevertheless, seeing that fowls, pigeons, and calves, as well as some domestic animals, are susceptible to the infection of human diphtheria, the possibility of a re-transmission of the disease to the human being cannot be denied and should not be overlooked.

Dr. Herman of Cape Town, answering my inquiries, has always found the disease in proximity to "manurial heaps and vegetable deposits," or to "cow stables." He points out that diphtheria, which is rather frequent "up country," appears in isolated farms in the sheep and cattle districts, where the animals are often herded in kraals, and where decaying refuse is not only in proximity to the dwelling-houses, but also close enough to contaminate the water supply.

Our own experience has long tended to confirm this view, first put forth in print by Renshaw, that diphtheria is especially apt to be associated with the proximity to heaps made up of both animal and vegetable refuse.

I have known three cases in which an outbreak of diphtheria in a household had been preceded by an attack in the families of

the coachman in adjoining stables. In another instance there was connection of the drainage from the stables with that of the house; and lastly, I was consulted with regard to a case in which the probable predisposing cause was proximity to a very insanitary pigsty.

With regard to stables, all medical superintendents of infectious fever hospitals would probably agree that diphtheria is very frequent among those who have to do with horses. Not only does this apply to those who live in stables, but to drivers and conductors of cabs, omnibuses, and tramcars. Nor does this association of diphtheria with stable workers appear to be much influenced by variations in excellence of stable sanitation.

No doubt, since manure pits have been abolished, and the heaps have been cleared away more frequently than formerly, the sanitary condition of mews is better than in former times; but one fact is worthy of notice in this connection—namely, that in the last 15 or 20 years the old practice of exchanging manure for fresh straw from the farms has fallen into desuetude, and as straw is now the more valuable, it is used for a longer time, and consequently the manure is allowed to remain until it is in a much further advanced condition of decomposition than formerly.

The following case, in which I was consulted by Dr. Poyntz Wright, medical officer of health for St. Neots, is a fair example of the influence of country life in the origin of diphtheria:—

A young lady, aged 24, had been subject to "ulcerated throat" and lacunar tonsillitis ever since she had scarlatina, fifteen years previously. Four days before her attack, the patient had walked across a turnip-field which had recently been flooded. She experienced great nausea from the horrible stench which was exhaled, but continued her walk to a sewage-farm, where she gathered some moss from an osier-bed. On the following day a sharp sickle-shaped herring-bone lodged in the left tonsil, and in her endeavours to extract it broke off short. Sore throat commenced two days later, and on the next—the fifth from her visit to the sewage-farm—membrane appeared. The exudation was strictly limited to the *left* side of the fauces, with the exception of *one small patch* of membrane on the *right* tonsil. On the sixth day there was complete paralysis of the velum on the left side, with paresis of the muscles on the right. A friend and other children of the same family who had been

walking with her on the occasion noted were unattacked; and with the exception of one (doubtful) case of diphtheria ten miles distant, the district was quite free from the disease.

There can be little doubt that in this case the chronically inflamed condition of the tonsils, and the consequent abeyance of their function of phagocyte-production, rendered the patient susceptible to the noxious influence of the probable microbic poison of the decaying turnips, and to possible germ emanations from the osier-bed at the sewage-farm, and that the wound from the herring-bone further prepared the throat to receive infection.

The following curious circumstance is worth recording in this connection, though it has points of interest which apply to other considerations of etiology; it has also an especial bearing on the prophylactic influence of antiseptic measures:—

I was asked, in July 1885, to attend a young lady in conjunction with Mr. Henry Bury, of Whetstone. The patient was a tall, well-grown girl of 17, and of good constitution. She resided in the same house as, and was the constant and inseparable companion of, another young lady of the same age, but of delicate health, who had for some years been under my constant care on account of strumous ozæna, for the relief of which she diligently employed antiseptic applications in the shape of sprays, douches, and ointments. There were other cases of diphtheria in the adjoining stables and in the neighbourhood, but the exciting cause in the case under notice was believed to be the breathing of exhalations from the stagnant and foul water of a pond where the two girls had been amusing themselves catching tadpoles, &c. Now the stronger of the two had diphtheria very virulently, and the attack was followed by grave and protracted paralyses. The delicate girl, who was employing antiseptics, had a very high temperature for two or three days, and was prostrated; but she exhibited no throat symptoms nor sequelæ whatever.

(*b.*) **Dissemination.**—While the foregoing causes may account for many an outbreak of diphtheria in rural districts, such as those referred to by Dr. Herman in isolated homesteads, it has been pointed out that the neighbourly inter-communication, which is the rule in villages, is infinitely more intimate and frequent than in large cities. This fact needs no elaboration; but interesting examples of its force are supplied in several of the Government Reports, which are here tabulated.

The increased facilities of transit and means of communication between those living in the country and those residing in towns, and the aggregation of children in Board schools and in other similiar institutions, have doubtless their share in the gradual equalisation of mortality in rural and urban populations. Some of these will receive fuller consideration. But besides and beyond these circumstances there are questions relating to the sanitation of large towns and cities, in regard to which Dr. Corfield has suggestively expressed doubts as to whether many of the so-called improvements in drainage, disposal of sewage, and ventilation of sewers are really improvements after all, but this is again to somewhat anticipate.

Geology.—According to Dr. Longstaff the greatest mortality from diphtheria has occurred in four especial districts, namely, Norfolk, Lincolnshire, North Yorks, and Sussex.

If we compare the geological features of these areas with others in which similiar conditions of strata obtain, it cannot be contended that there are any conclusive data to be derived from a geological point of view, which can be held to exert an appreciable influence on the development or on the diffusion of diphtheria. And this conclusion is strengthened by a comparison between counties such as Herts and Bucks, which possess similar geological features to those existing in Norfolk. While, however, the mortality ranges from 54 to 79 in the former two districts, in Norfolk it is 149 to 191.

It will thus be seen that epidemics in our country have been very catholic in their distribution from both the geographical and the geological aspect. Nevertheless, our table would appear to justify the belief in a decided preference of diphtheria for a clay soil, an excess of diphtheria on argillaceous strata in the United Kingdom being evinced to the extent of 57·7 per cent. These figures bear out the opinion of Dr. Thorne Thorne that " where a surface soil is, by reason of its physical constitution and topographical relations, such as to facilitate the retention of moisture and of organic refuse, and where a site of this character is, in

addition, exposed to the influence of cold and wet winds, there you have conditions which do tend to the fostering and fatality of diphtheria, and also go to determine the specific quality of local sore-throat." Also that of Dr. Airy, who refers to "diphtheria in its favourite haunts on clayey soil," affirming that the "soil was in almost every case (inspected by him) more or less clayey and wet." Dr. Kelly also points out that "the mortality from diphtheria is much higher on wet and retentive soils than on dry and pervious ones." Nor does it appear to make much difference whether the clay is on the surface or lies below a porous upper stratum such as gravel, green sand, sandstone, oolite, &c.; for any such strata deposited on clay produce a water-logged condition, than which there can be none more favourable for the growth of the lower forms of vegetable life; and this brings us to recognise that dampness of soil implies, even with the best laid schemes of drainage, a dampness of habitation, the specific connection of which with diphtheria Thursfield was one of the first to enforce.

Diphtheria has been noticed to be more or less endemic in riverside villages, where the cottages are much enclosed by trees and covered by floral vegetation.

Outbreaks of diphtheria have occasionally been manifested in bleak, exposed and cold situations, as on heaths and high elevations; but here probably a tendency to sore-throat from the action of keen winds has been an alternative predisponent of infection, to the more usual low type of inflammation resulting from damp.

Rainfall.—The amount of rainfall differs to an appreciable degree in the United Kingdom, according to the geographical situation of any given locality. In the eastern counties the average is below 25 inches per annum; in Westmoreland, Cumberland, Wales, and the most elevated parts of Devonshire it may vary between 60 and 200 inches; and in the remaining parts of England the average is usually between 30 and 40 inches yearly. Professor Ramsay gives the following averages for the amount of

rainfall per annum:—Cornwall, 37 to 54 inches; Sussex, 26·3 to 29 inches; Norfolk, 24 to 25 inches. In the higher parts of Yorkshire, 51 to 56 inches.

The rainfall in the western part of England and Wales is greater than that in the east, gradually becoming less as we pass from the S.W. to the S.E. areas, a fact which bears no relation to the areas where diphtheria is stated to be most prevalent. In view of these statistics, therefore, the relation between outbreaks of diphtheria and excessive rainfall is by no means evident, for, to take one more example,—while in Lancashire, the average rainfall is from 60 to 64 inches, the diphtheria mortality is as low as 54 to 79; in Norfolk, which has an average rainfall of 24 to 25 inches, the diphtheria mortality rises to 149 to 191.

Oertel's remarks on aerial infection of diphtheria are worthy of quotation. He says:—"The possibilities of its transport are so many that they cannot always be shown even by the most careful inquiry. Transport by the atmosphere is rare, and one should only accept that explanation when really compelled to exclude all means of direct transport. Moreover, it cannot be denied that the sudden and simultaneous outbreak of many cases of diphtheria in one locality points rather to an infection either by direct contact or by means of handling the same objects than to an infection by means of air and water. For those epidemic and infectious diseases, for which we are compelled to admit the last-named mode of propagation, differ from diphtheria in that they are characterised by a gradual spread of the epidemic, which epidemic proceeds from single cases."

But we must consider that we are definitely required by the hygienic and sanitary aspect of the case to remember that the air and water may act as carriers of the virus. Not, of course, in the same sense as the air of a malaria-region may be the constant bearer of the malaria-poison, or a contaminated well may be the source of an epidemic of typhoid. In the case of diphtheria, air and water can only act in the sense of actually carrying the contagion from one person to another, just as clothing, cooking and

other utensils, or even such things as victuals, bread, milk, furniture, ornaments, and wall-paper. All that has been said of the poison arising in damp houses and specially situated localities rests more on the knowledge that such places are especially apt for the development of all kinds of fungoid growth, than on any reason which would satisfy a more stringent inquiry.

Season.

The disease is certainly more frequent in cold damp weather, and in the months comprised from the fall of the year to the spring. It is especially prevalent during the months of October and November, when the atmospheric conditions are favourable to the development of fungoid germs, and to catarrhal inflammations generally; but it cannot be denied that diphtheria occurs at any period of the year, and under very varying influences of wind and weather. Diphtheria is far more frequent in temperate than in tropical climates, but in the latter it is by no means unknown.

An interesting example of the liability to draw false conclusions with regard to the influence of the weather on diseases of the throat, is afforded in a report issued by one of the London Medical Officers of Health for the summer quarter, 1893, in which belief was expressed that an increase which had been observed in cases of throat-inflammation of an insanitary type, consequent on long continued drought and heat, was referable, *First*, to the wind-carrying of dried pathogenic organisms in the form of dust, and *Secondly*, to the want of proper flushing of sewers.

We were, however, enabled to show by figures compiled on a large scale, that it is *not during* dry weather that throat diseases of this character are most prevalent, but on the first occurrence of a light rainfall after a prolonged heat and drought. In other words, that the epidemic wave seems to be greatest when the first rainfalls, being but slight, are sufficient to stimulate the dry and comparatively inert organic matter to activity, and that the prevalence only diminishes or disappears with the thorough

flushing of the sewers, consequent on heavier and longer-continued showers.

Domestic Surroundings.

Those who are well read in the history of diphtheria, as it has appeared in England in the last 40 years, cannot but be impressed by the fact that the districts which have been invaded during the last 12 years—as shown by our table—representing such different characters of soil and climate as Norfolk, Sussex, and North Yorkshire, are in many instances the same as those which were most seriously affected by the epidemic of 1855-60: and of several of these localities it may be said that they have never since been quite free.

It is evidence of this kind which has led to belief (probably misplaced or exaggerated) in the existence of some constant factor in the way of climate or geological formation; for, presumably, preventable causes have, at least in some instances, been corrected.

We must therefore seek for some further cause than that of soil, and it is fair to suspect that in most cases a solution of the doubt would be found in variations in sanitary environment.

In estimating the preponderating cause assigned to the various outbreaks enumerated in the table, one is forced, by a consideration of the data given, to arrive at the conclusion that the inferences drawn from these reports by the various inspectors—carefully worded as they are—are not always in consonance with the facts. And, as a result, it has become fashionable to ignore the importance of those conditions in regard to diphtheria which are held to be of etiological value in the case of all other zymotic diseases; and to assign, somewhat fancifully in many instances, causes for the origin of an outbreak, which should be more properly considered as causes of dissemination.

Our contentions are:—

(1) That insanitation is one of the strongest predisponents not only to "simple sore throats," membranous and non-membranous, but also to true diphtheria.

(2) That in cases of diphtheria attributable to contagion or importation, the infection-element is highly influenced in its development by non-hygienic conditions of individual or local surrounding.

And lastly, that such non-hygienic conditions are not only responsible for the development of diphtheria, but that they do unfavourably influence the gravity of an epidemic or of an individual case.

For we find that in 42 out of the 45 Local Government Board reports—that is, in 93·3 per cent.—there were undeniable evidences of defective sanitation, although in 29 only, 64·4 per cent., is such a cause assigned by the medical inspector for the origin of the outbreak.

The nature of the assigned causes of the inspectors and of the actual state of sanitation under the various headings for consideration may be classified as follows :—

Cases due to Insanitation or Polluted Water, . .	29
„ „ Infected Milk Supply, . . .	4
„ „ Contagion in Schools, &c., . . .	11
„ „ Doubtful, ...	1
	45

The general condition of Drainage and Sewerage was :—

Defective, or even absent, in	42
Good or fairly good in	2
And not imputed in	1
	45

Chief amongst insanitary causes are impurity of drinking water and milk, the taint of the last being, as will be presently shown, usually due to dilution with impure water or to cleansing of the pails with the same; defective sewers, ill trapped drains leading to an escape of sewer gas, surface ventilation of main sewers, soakage of soil with sewage poison, and indeed all those conditions

considered favourable to the development of typhoid fever and scarlet fever, with which diphtheria has so many points of resemblance.

Strong as is the evidence against a *de novo* origin of any of these infectious diseases, it is held by some as unnecessary that the poison arising from any of the causes named should invariably be that of diphtheria. Nevertheless, in all probability such is generally the case, and the discovery of a separate bacterium for each variety of infectious fever can only be a matter of time.

In the cases assigned to **Infected Milk** we find that three epidemics out of the four were associated with grave defects in the drainage of the locality where the outbreak occurred; and, altogether, notwithstanding "anecdotal" evidence, it is doubtful if milk, *independently of outside contamination,* is by any means a frequent agent in the propagation of diphtheria. For in only one case in our table, No. 16, that of Ealing in 1887, does it appear to have been the sole cause.

Even here, although the inspector believed that there was "a very strong presumption that the milk distributed from the dairy in question did, somehow or other, have to do with the outbreak of diphtheria, there is nothing amounting to proof of this, and on the other side an explanation is wanted of a notable disproportion between the quantity of milk distributed by the suspected dairy, and the amount of diphtheria witnessed among its customers."

To take another report, No. 4 in our table, which treats of an epidemic of diphtheria in Hendon in 1883, analysis of a "sample of milk from the particular dairy that came in question, and a sample of the pond water there used for farm and dairy purposes, failed to find any fault with the milk," while the water was "discovered to be fouled to a large extent by sewage matter, and to contain in abundance, animalculæ which were visible to the naked eye."

There was a complaint made of a "ropiness" in the milk, but this was not observed when it was drawn off in carefully washed

glass vessels, nevertheless there is a tendency on the part of the inspector to impugn the milk rather than the water used to cleanse the pans and pails.

With regard to defects of sewerage being responsible for this outbreak, as well as for a certain amount of endemicity in the district, the inspector writes, "upon this point I need only say that, given a sewer origin of diphtheria, the circumstances of the sewerage in Hendon are likely to foster it."

The report (No. 3 in the table) on an outbreak which took place about the same time at Devonport, appears still more conclusive of secondary contamination of the milk as distinguished from impurity due to cow disease, as the following abstract from the report will show :—

The residents at the milk shop—dairyman, wife, two sons, and a servant, all adults, were stated to have been in good health. Next door, however, a case of diphtheria had occurred recently. The houses were much enclosed, and a communication was proved to exist between the drains of the dairyman's house and the W.C. next door. The milk cans, instead of being drained dry, were wiped with cloths which hung in close proximity to these ill-ventilated drains.

To make our position quite clear in this matter, it is necessary to refer to one more epidemic of diphtheria, namely, that which occurred in 1878 in Kilburn and St. John's Wood, but is not included in our table. The report referred to 264 cases, with 38 deaths, a mortality so disproportionately small as to practically prove that but a small number, if any, of the cases were truly diphtherial. Sore throat was endemic in the district. All causes were set aside except that of sewers and drains, and these were found to be generally badly ventilated and inadequately flushed, with, in several instances, direct communication between cisterns and baths with the drains. There was also an obstruction in the main sewer and a backward flow. Notwithstanding all these facts, the reporter, although he did not deny that the "sewer defects" theory had some *primâ facie* justification, endeavoured to

prove that sewerage held at best only a secondary and subordinate place in the causation.

The evidence supporting the milk theory rested almost entirely on the statement of interested persons, and absolutely no testimony is afforded of any disease in the cattle.

The foregoing facts, which could be amply corroborated by an examination of reports of other outbreaks attributed to infected milk, fail to carry conviction against this particular and valuable article of food.

It must, however, be admitted that milk is a congenial soil for the growth of micro-organisms—the diphtheria bacillus included—at a low temperature, and therefore it cannot be denied that this fluid may become a medium of infection. But it has also to be noted that the bacillus when grown in milk loses many of its chief characteristics, or perhaps it would be more correct to say it assumes others peculiar to its culture medium. It probably undergoes degenerative changes with rapidity; possibly these are due to the presence of lactic acid.

In the eleven epidemics assigned to **contagion** and **importation**, the whole were found to be associated with sanitary defects of some kind. In one case diphtheria was said to be endemic, and in addition, in six cases reported as mainly due to insanitation, **dissemination by schools** was also noted.

Emanations from **accumulations of organic and other refuse** which were foul and offensive were reported in nineteen cases (42·2 per cent.), and the outbreaks were associated with **scarlet fever, measles, enteric fever,** or "**simple sore-throat**" in nine cases, otherwise to the extent of 20 per cent.

In connection with foul emanations as a cause of diphtheria, it may be noted that the opinion has recently become prevalent that the ventilation of sewers on the street level, and the disposition of small children to play about the gully-holes, may in some measure be responsible for the increased prevalence of diphtheria in urban over rural districts, the converse having been formerly the case.

It may be, as has recently been reported, that experiments fail to prove the presence of a bacillus in sewer gas, and we give every respect to Koch's statement that these microbes "cling to their moist bed," and "cannot pass spontaneously into the air from a moist surface." Nevertheless the every-day experience of practitioners of medicine is overwhelmingly in agreement with the *direct* connection between the inhalation of foul gases and the occurrence of diphtheria and other specific infectious diseases.

However that may be, it appears as imperative on us to convey the ventilation pipes of public sewers above the level of ordinary respiration, as is admitted to be the case in relation to the ventilation of water-closets in private houses; and it is worthy of note that certain cities in which ventilation of sewers is not employed, have been found to be singularly free from outbreaks of diphtheria. On the other hand, a case has been reported in which an epidemic in the suburbs appeared to be promptly checked after flushing sewers so ventilated with a powerful germicide solution.

A medical officer of health in a large suburban district has recently expressed the opinion that the increase of diphtheria in urban communities has been consequent on the introduction of water-closets and the draining of houses into sewers; he supports his contention by quoting from so powerful an authority as Dr. Vivian Poore.

Nevertheless, the arguments which he employs tend rather to show that the connection between the two circumstances is due more to imperfections in the closets themselves and leakage in the drains than to the system.

The accumulated evidence of the various insanitary conditions which is here tabulated, and has been reviewed at length, can hardly fail to convince the impartial observer, that (to quote Sir George Johnson) "not to recognise the frequent filth origin of diphtheria may in practice be as disastrous as to ignore its infectiousness."

TABULAR ABSTRACT OF REPORTS TO THE LOCAL GOVERN-

No.	Inspector.	Date.	District.	Geological formation.	Principal Cause Assigned.
1	Dr Parsons	Dec. 26, 1882	Gedney Drove End (Norfolk)	Clay soil	Doubtful; wind current suggested
2	Dr Airy	Jan. 23, 1883	Coggeshall (Essex)	Gravel over clay	Probably polluted water
3	Dr Parsons	Feb. 1, 1883	Devonport (Devon)	Limestone and slate	Infected milk
4	Mr W. H. Power	Apr. 5, 1883	Hendon (Middlesex)	Clay	Infected milk
5	Dr Airy	Aug. 20, 1883	Great Dunmow (Essex)	Gravel	Insanitation
6	Mr W. H. Power	Mar. 8, 1884	Tichmarsh (Northampton)	Oolite and clay	Insanitation
7	Dr Parsons	Mar. 24, 1884	Hambledon (Hants)	Chalk	Polluted water by sewage
8	Dr Parsons	May 12, 1884	Eversholt (Beds)	Green sand and clay	Contagion
9	Dr Blaxall	May 15, 1884	Kingsclere (Hants)	Sandstone, chalk and clay	Contagion; school influence
10	Mr R. D. Sweeting	Jun. 29, 1885	Cheshunt (Herts)	Gravel and loam over clay	Contagion; school influence
11	Mr R. D. Sweeting	Aug. 3, 1885	Kempston (Beds)	Oxford clay	Contagion
12	Dr Gresswell	Aug. 7, 1885	Glanford-Brigg (Lincs)	Clay and chalk	Insanitation
13	Mr R. D. Sweeting	Aug. 29, 1885	Great Ousebourne (Yorks)	Sandstone and clay	Contagion
14	Dr Gresswell	Apr. 2, 1886	Beddington (Surrey)	Sandy loam and chalk	Insanitation
15	Mr W. H. Power	Apr. 7, 1887	York Town and Camberley (Surrey)	Bagshot sands	Infected milk
16	Mr W. H. Power	May 31, 1887	Ealing (Middlesex)	Clay	Infected milk
17	Dr Parsons	Aug. 4, 1887	Pwllheli (Carnarvon)	Limestone	Insanitation
18	Dr Airy	Aug. 12, 1887	Haslemere (Surrey)	Sand and clay	Insanitation
19	Dr Parsons	Mar. 7, 1888	Wincanton (Somersetshire)	Lias clay	Insanitation
20	Dr Bruce Low	Apr. 23, 1888	Enfield (Herts)	Gravel and clay	Insanitation
21	Dr Airy	July 3, 1888	Uckfield (Sussex)	Sand and sandstone	Contagion
22	Dr Blaxall	Sep. 4, 1888	Midsomer-Norton (Somersetshire)	Red marl and clay	Insanitation
23	Mr Spear	Oct. 26, 1888	Dingestow (Mon.)	Clay and red sandstone	Insanitation
24	Dr Bruce Low	Oct. 31, 1888	Ashbourne (Derbyshire)	Red sandstone	Insanitation
25	Mr Spear	Dec. 5, 1888	Aylesbury (Bucks)	Oolite, Portland stone and clay	Insanitation
26	Dr Page	Dec. 8, 1888	Berwick-on-Tweed	Clay and sandstone	Insanitation
27	Dr Airy	Dec. 12, 1888	Norwich (Norfolk)	Gravel and chalk	Insanitation
28	Dr Ballard	Feb. 18, 1889	Camelford (Cornwall)	Sand and slate	Insanitation
29	Mr Spear	Apr. 23, 1889	Fareham (Hants)	Sand, chalk and clay	Insanitation
30	Dr Bruce Low	July 9, 1889	Halstead (Essex)	London clay and chalk	Contagion; school influence
31	Dr Parsons	Sep. 2, 1889	Sowerby Bridge (Yorks)	Sandstone	Insanitation
32	Mr Spear	Sep. 6, 1889	Penistone (W. Yorks)	Sandstone and clay	Insanitation
33	Dr Bruce Low	Dec. 2, 1889	East Haddon (Northampton)	Limestone and clay	Insanitation
34	Dr Parsons	Dec. 21, 1889	Leek (Staffordshire)	Sandstone and limestone	Insanitation
35	Mr Spear	Mar. 29, 1890	Tredegar (Mon.)	Ferruginous sandstone	Insanitation
36	Dr Blaxall	Apr. 1, 1890	Berkhampstead (Herts)	Chalk	Insanitation
37	Dr Bruce Low	July 21, 1890	Barnstaple (North Devon)	Sand and limestone	Insanitation
38	Dr Bruce Low	Sep. 8, 1890	Malmesbury (Wilts)	Oxford clay	Insanitation
39	Dr Horne	July 10, 1893	Derry hill (Wilts)	Limestone	Contagion; school influence
40	Dr Horne	Oct. 28, 1893	Usk (Mon.)	Sandstone and limestone	Insanitation
41	Mr R. D. Sweeting	Dec. 11, 1893	Alton (Hants)	Chalk	Contagion; school influence
42	Dr Wheaton	Mar. 30, 1894	Hinkley (Warwickshire)	Clay and sand	Contagion; school influence
43	Dr Evan Evans	Apr. 27, 1894	Rainham (Essex)	Sand and clay	Insanitation
44	Mr T. W. Thompson	Nov. 22, 1894	Barnham Broom (Norfolk)	Boulder clay	Insanitation
45	Dr Bruce Low	Nov. 27, 1894	Hastings (Sussex)	Green sand and clay	Insanitation; importation

MENT BOARD ON OUTBREAKS OF DIPHTHERIA, 1882 TO 1894.

Drainage and Sewerage.	Water Supply.	Privies.	Refuse Accumulations. Remarks.
No system; cess-pools foul	Wells defective and polluted	Defective	Offensive vegetable matter
Defective	Polluted	Too near dwellings	Associated with wet season and poverty
Defective; sewer gas	Good	..	Contamination probably by foul wiping-cloths for milk cans
Defective and in-sufficient	Pond water polluted with sewerage	..	Invaded houses were the best in district
Defective water-closets	Wells polluted by sewerage	Too near dwellings	Possible connection noted with convalescent scarlatina
No sewerage at all	Wells polluted	Foul and offensive	No evidence of "foreign importation"
Very bad	Polluted in wells	Offensive and defective	Possible connection noted with scarlatina
No system of drainage	Good	Pail closet; cesspit over-full	Mild scarlet fever and measles in spring
No sewers	Exposed to pollution	Offensive cesspits	Outbreak probably introduced by teacher
Not imputed	Liable to pollution	Privies foul	Outbreak commenced with epidemic of "simple sore-throat"
No drainage	Exposed to pollution	Defective	Offensive refuse
Very defective	Deficient and bad quality	Defective and foul	Personal communication leading to dissemination. Foul heaps
Defective	Polluted by surface matters	Midden privies, uncemented, &c.,	Foul refuse abounds; sewer emanations abundant
Defective	Good	..	..
Atmosphere sewage tainted	Good	..	Banks of mud and sewage sediment from river-cleansing
Good	Good	..	No evidence available as to the source of infection
Very defective	Impurity suspected	Defective	Heaps of offensive organic refuse
Very defective	Exposed to pollution	Very Defective	Formerly offensive house refuse
Bad drains; leakage	Wells polluted	Defective and offensive	Offensive domestic refuse
Defective	Unwholesome	Defective	Offensive refuse
Defective	Some sources bad	Faulty	Outbreak followed on heat and drought
Very defective	Exposed to pollution	Bad	Foul animal refuse
Absent or very bad	Polluted	Defective and primitive	Adults suffered disproportionately
Very defective	Liable to pollution; often foul	Foul	Foul emanations from abundant slaughter-houses and pig-styes
Drains foul and defective	Fairly wholesome	Foul and offensive	Streets badly paved, unchannelled and unscavenged
Imperfect and defective	Inadequate	Insufficient and unwholesome	Ditto ditto
Drains foul and defective	Liable to pollution	..	Dissemination by schools also noted
Bad and neglected	Polluted	Offensive	Heaps of highly offensive excrement
Drains foul; very bad	Polluted	Foul and defective	Sporadic diphtheria long prevalent, and associated with enteric fever
Fairly good	Fairly good	Foul and defective	Very offensive smells from slaughter-houses
Drains defective	Said to be pure	Defective closets and privies	Infection through school also noted
Foul and defective drainage	Polluted	Foul and offensive	Associated with enteric fever
Very defective	Polluted	Foul; too near dwellings	Outbreak aggravated by bad weather
Very defective	Exposed to pollution	Foul and defective	Associated with scarlet fever
No system whatever	Bad	Insanitary	Buildings unfit for habitation (Abstr. from *Brit. Med. Jour.*)
Very defective	Polluted	Defective	Refuse and pig-styes close to dwellings
Very bad	Liable to pollution	Foul and defective	Offensive refuse
Very defective	Polluted	Foul and offensive	Accumulations not removed
Absent	Wells foul	Primitive	Diphtheria more or less endemic
Imperfect	Surface contamination	Foul and offensive	Manure heaps near dwellings (Abstr. from *Brit. Med. Jour.*)
Not adequate	Said to be good	Defective	Marked absence of sanitary precautions
Very defective	Said to be pure	Closets defective	Offensive offal refuse
Defective	Often polluted	Very defective; often foul	Offensive refuse heaps
Defective	Often polluted	Defective	Diphtheria following measles
Defective	Fairly good	Defective	Antecedent and concurrent scarlet fever; also small-pox

Preceding or Concurrent Epidemics.

In the case of an epidemic of typhoid fever it is not difficult to determine the nature of the disease and the type in which it is exhibited by an examination of a few cases, but this is very different in a prevalence of diphtheria, which, beginning with a few cases of mild sore throat, may develop into an epidemic of the greatest malignancy, and during its rage cases may be exhibited in very varying degrees of intensity and infectiousness according to age and other individual circumstances. Moreover, a large proportion of outbreaks of diphtheria are preceded by, or run concurrently with, epidemics of other specific fevers. These facts have been recently enforced by me as a reason why the proposals of the Local Government Board in regard to more exact examination of a few cases at the commencement of future epidemics of diphtheria cannot be placed on all-fours with those relating to typhoid fever and some other diseases, of which the cause has long been definitely ascertained and accepted.

The frequency with which diphtheria is associated with **scarlet fever** is well known, but its relation to **measles** is by no means so generally recognised. Ryland mentions it in his Jacksonian Essay in 1837, and Dr. West in 1843. The following facts, taken from one of the most recent reports to the Local Government Board, are of interest in this connection. Mr. P. W. Thompson, reporting on an outbreak of diphtheria at Barnham Broom, near Norwich, No. 44 on our list, and dated November 22nd, 1894, remarks :—" I find from my notes that, with one or two exceptions, all the children who, later, suffered from diphtheria, had about this time suffered from **measles**, which in some cases had been attended with considerable soreness and external swelling of the throat. The frequency with which diphtheria is found to coexist with or quickly follow in the wake of measles is such as to suggest a relationship between the two phenomena; though the relationship may be of an indirect kind only, the measles increasing susceptibility to diphtheria, mainly, in all

likelihood, by the damage inflicted on the mucous membrane of the throat."

A lady who had read some communications which have appeared recently in the public press on this subject writes to me to the effect that five years ago her two little sons were attending a school in the west end of London. The eldest boy began with an attack of tonsillitis, on which measles supervened. Several cases of measles had occurred among the pupils at the school, and had been followed in many instances by diphtheria, but this had not been notified by the head-master to the parents. The boy had a croupy cough and symptoms of dyspnœa, but with ill-developed rash; he recovered, but his younger brother took the measles, with subsequent diphtheria of a malignant type, from which he died. His father was attacked by diphtheria, and also died. Two of the three trained nurses in attendance suffered from diphtheria, and were dangerously ill for some time: a Swiss servant also nearly died from the same cause; and finally, a week later, the housemaid was attacked, and died. Five of the pupils attending the same school as this lady's sons died. A long investigation by experts failed to account for the outbreak.

Reverting to **scarlet fever**, Dr. Bruce Low, in a recent report (the last in our table) on the prevalence of diphtheria in Hastings, says "that the two diseases, in certain instances, were concurrent, and a number of persons who, on account of their suffering from scarlet fever, were sent to the borough sanatorium for isolation and treatment, were attacked by well-marked diphtheria during their convalescence," and several examples are given "of importation of diphtheria into families by members returning home from the sanatorium after recovery from scarlatina, the patients in each instance not having been known to suffer from diphtheria during stay in hospital."

This same report states that, six months previous to the final disappearance of diphtheria in the district, **smallpox** appeared, and that some of the patients who were in the sanatorium for treatment from scarlet fever were attacked with the disease. Nevertheless, we find no mention of any case of diphtheria occurring in connection with the variola. Personal inquiry from Dr. Scarlyn Wilson, the medical officer of health, confirms the impression that during this outbreak of smallpox there was nothing in any of the patients to suggest co-existent diphtheria.

Information specially furnished to me as to the occurrence of diphtheria in connection with smallpox convinces me that it is most rare. Dr. William Gayton, who has had an experience of 15,000 cases of variola, states that he has never seen one; and Dr. Carnall, the present resident medical officer of the Smallpox Hospital, also informs me that the records are blank on the subject, and that, as smallpox is now seen, laryngeal complications are not common, except of a mild form. Nevertheless, three cases of reputed diphtheria after variola, which occurred in that institution at the time of the outbreak of 1856-60, are related in Mr. (afterwards Sir John) Simon's second report to the Privy Council in 1860, on the authority of Mr. Marson, who was for many years superintendent of that hospital. The late Dr. Heslop of Birmingham also reported a case of confluent smallpox, in which a diphtheritic exudation was observed.

These cases having occurred before the days of bacteriology, cannot be accepted as undoubted examples of true diphtheria.

Much the same may be said in regard to **typhoid fever**, which, being a disease often accompanied by stomatitis and faucitis of a pseudo-diphtheric character, is doubtless one offering a fertile soil for the implantation of the true diphtheria bacillus.

The facts that outbreaks of diphtheria so often occur in districts where enteric fever is endemic, as well as the many points of parallelism in the clinical history of the two diseases, are significant.

An epidemic of diphtheria has recently been reported at the Aubervilliers Hospital in Paris, which occurred among the patients attacked with **chickenpox**. They were completely isolated, so that contact with any other patient was impossible. Not one of the chickenpox patients, when admitted into the hospital wards, exhibited false membrane in the throat. There was no case of diphtheria in the hospital. It was supposed that the diphtheria bacillus might possibly have been present in the saliva of one of the patients in the ward, and, moreover, that it might have been also possible that the individual who carried the bacillus may not

have had diphtheria. Nor is this the only example which might be quoted.

Where diphtheria is not associated with an actual specific fever a prevalence of some less serious form of infectious sore throat is a frequent feature, and this is so not only in our present tables; for, referring to Sir John Simon's report to the Privy Council in 1859-1860 on the earlier outbreaks, we find that of 29 epidemics of reputed diphtheria distributed over various parts of the country, **endemic sore throat** was noted in 27 cases, while in more than half there was a marked tendency to **tonsillitis**; and finally, in 23 instances there was association with **scarlet fever.**

Constitutional Predisposition.

Sir William Jenner speaks strongly of "the influence of family constitution in favouring the occurrence and determining the ending of diphtheria," and quotes several cases of multiple attacks in the same household, "in all of which the hygienic conditions were good: there was nothing patently bad in regard of drainage, ventilation, overcrowding, water supply, food, or work. All the patients were in the middle rank of life, and resided in good-sized houses, and in fairly open situations. These facts, of course, speak strongly in favour of contagion, as well as in favour of the influence of family constitution"; but even with this allowance, facts in support of Sir William Jenner's opinion as to the influence of constitution are not wanting.

First and foremost, one must place that constitutional state which, running in families, tends to the development of those conditions which combine to produce what is known as **mouth-breathing** and their effects. In such a child the air, instead of being taken through the nostrils, where it is warmed, moistened, and filtered, goes direct to the throat—cold, dry, and germ-charged.

Chief among the causes of obstruction of the naso-pharyngeal passages are **enlargement of the faucial tonsils** and hypertrophy

of Luschka's tonsil, otherwise known as **adenoid vegetations**; and as results we find a strongly expressed "catarrhal" disposition along the whole upper respiratory tract, from a chronic cold in the head to frequent attacks of laryngitis and bronchitis. The well known impeded development of the chest walls in mouth-breathing children is also responsible for pulmonary disorders of a recognised type.

My personal experience leads me to say that diphtheria hardly ever, if ever, occurs in a child under seven years of age who is not the subject of one or other of these forms of glandular overgrowth. It appears needless to enforce their tendency to abrogate the hygienic functions of the nose as the first avenue of respiration

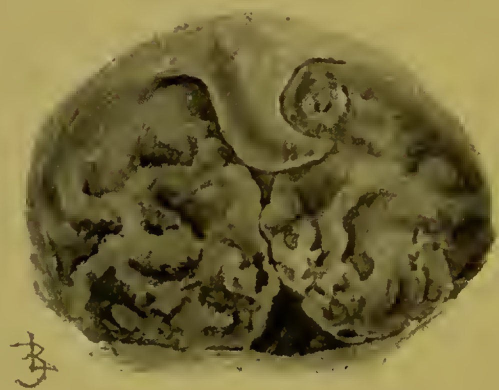

Fig. 1.

and to induce the marked deficiency in vitality and resisting power to contagion which are to be found in all such children.

Indeed, this fact alone might account almost entirely for the varying death-rate from diphtheria according to age; since puberty is equally the period when tonsillar overgrowth has a natural tendency to reduction, and the mortality from diphtheria to markedly decrease. In many cases of diphtheria in young adults tonsillar enlargement will be found to have persisted; and it has been particularly noted in nurses who have taken the disease.

The accompanying illustration (Fig. 1) is the tonsillar portrait of a nurse (aged 22) in an infectious fever hospital, taken some two months after she had passed through an attack of diphtheria. The tonsils were removed, at the Central Throat and Ear Hospital,

with marked advantage to her general health, and she resumed her duties as a diphtheria nurse.

Moreover, we have experience of several cases illustrating this point in a two-fold direction—namely, some in which removal of enlarged tonsils, and the consequent restoration of normal nasal respiration, have appeared to give a special immunity to the disease; and others in which advice as to the removal of these glands and accompanying adenoids having been neglected, diphtheria has been specially fatal. Lest this statement should appear to be an exaggeration, it may be remarked that, in 1000 consecutive cases of diphtheria specially tabulated for this essay, the exudation was reported to be **limited** to the **tonsillar region** in **666 cases**, and that in **only 8 of the 1000 was it not implicated.** The fact of **99·2 per cent.** of manifestations of diphtheria in this region is one the importance of which cannot be too strongly enforced.

Not only is diphtheria highly contagious to those in attendance on the stricken patient, but its infecting properties may be retained for months, and even years, in tainted clothing, dwellings, and apartments.

By what agency a medical attendant, a nurse, or other person in attendance, where every precaution against infection is taken, contracts diphtheria by merely breathing the same atmosphere as the patient—for only a few minutes, it may be—it is difficult to explain; though doubtless it might be advanced that in most of such cases the conveyance of contagion is more material than is often admitted. There are, however, many isolated cases which can only be explained by supposing that germs from a diphtheric patch contaminate the breath.

Research into modern literature has failed to find any record of experiments in this direction, such as have been pursued with regard to the breath conveyance of the tubercle bacillus. Having regard to the more superficial position of the diphtheria bacillus, there would be reasonable hope that an attempt would be successful.

In this connection the question might arise, Why, if the oral secretion form a suitable culture medium for the multiplication of the organisms (an essential feature in the infecting process), is it that the mucous covering of the tonsils and other lymphoid masses are most usually the areas invaded by the microbes? In answer to this query, it may be pointed out that the tonsillar mucous membrane is more pervious to living organisms than any other, because of the diapedesis of leucocytes which is continually going on through it. Moreover, the crypts of the tonsils form quiet recesses for the incubation and subsequent germination of microbes, the whole constituting the "open wound" which Virchow has declared the tonsil to be. It is probable that in most instances where those exposed to infection have not contracted the disease, the leucocytes secreted by the tonsils have checked the germination of the organisms. Where, on the other hand, the tonsils are diseased, phagocyte production is diminished, and such individuals are more liable to contract the disease when exposed to infection.

Amongst the reports on outbreaks of diphtheria which have been abstracted, it has been remarked in one that a very large proportion of children attacked with diphtheria are the subjects of **decayed** and **badly-kept teeth**. This is probably true, but it is also true that this unhealthiness of the mouth and gums is a direct result of mouth-breathing, as is also the liability to enlarged **tuberculous**, or as they used to be called, **strumous glands** in the neck. It is interesting to note here that Trousseau had, so far back as 1843, devoted one of his lectures to "*La Diphthérite Gingivale et ses rapports avec le Croup* (Laryngo-Tracheal Diphtheria)," especially as regards its transmission. Bretonneau, in his *Fifth Memoir*, expresses the belief that the Empress Josephine contracted the malady to which she succumbed "from the gingival diphtheria of Queen Hortense."

Other constitutional predisponents have not been found in ponderable proportion, but the following quotation from my book may not be inappropriate:—"No doubt, an anatomical explanation—viz., the small and chink-like glottis of children—will account

in some degree for the high infantile mortality, but it is also probable that the delicate organisations of the young are more affected than in the case of an adult by the virulence of the poison, be it a ptomaine or what not; and I would once again repeat the opinion already frequently expressed, that in young children there is a greater tendency for inflammations of the air-passages to assume an exudative membranous type—thrush, plastic bronchitis, and non-specific membranous laryngitis being diseases almost entirely confined to the period of childhood and adolescence."

These remarks would naturally lead to consideration of the etiological influence of **age** on diphtheria, but as this question is very fully treated in a later section ("The Elements of Prognosis"), no further allusion is required, except to remark that diphtheria is pre-eminently a disease in which susceptibility to infection is in direct proportion to the youth of the individual.

Inoculability.

Trousseau and others having failed in certain experiments made on themselves and on rabbits, the inoculability of diphtheria was at one time disputed. There is now, however, no doubt that the disease can be transmitted by the application of necrosing membrane to mucous or abraded cutaneous surfaces.

The number of medical victims of the heroic, but none the less reprehensible practice of extracting membrane through tracheotomy tubes by their own lips instead of applying artificial suction is a striking testimony to its direct contagiousness. The failure of the experiments of Trousseau and others just alluded to can be readily explained by our own view; first, that diphtheric contagium requires a suitable *nidus*, or soil, for its development; and secondly, that all stages of the exudation are not equally active in their infective capability.

Our first proposition will be readily conceded, and is proved in a measure by the happy miscarriage of Trousseau's rash experiments

on himself. The investigations of Renshaw confirm the second, for the fact that many animals, especially the carnivora, can be infected by inoculation with a portion of diphtheric membrane has been abundantly proved; and the author just named has conducted a series of highly interesting experiments, of which the following is a brief *resumé*. Portions of greyish-white membrane were mixed with the food of six cats, and in every case the disease was reproduced with the characteristic lesions and symptoms. Experiments on fourteen cats with the younger yellowish-white membrane and with greyish membrane which had been soaked in Condy's fluid or in hydrochloric acid produced only negative results.

Experiments on these lines have been repeated by other observers, and with similar results.

Points of interest with regard to inoculation of the specific organism and its toxic products will be considered more fully in the succeeding chapters.

Contagion and Dissemination.

As to ward contagion, given sufficient air-space and ventilation, with strict attention to the disinfection of a patient attacked, it is doubtful whether diphtheria is communicated from bed to bed —unless exceptionally.

Of this one may assure himself by witnessing the course of events regarding the many patients who, having been admitted, on outside notification, to the diphtheria wards of our infectious fever hospitals, have been found not to be suffering from the disease for which they were received. Superintendents of these hospitals, of long experience, all agree that the liability of such patients to develop diphtheria is practically *nil*; and the fact cannot fail to modify generally accepted views regarding the infectiousness of the disease when uninfluenced by insanitary surroundings. On the other hand, it is unfortunately quite frequent for nurses who come *in contact* with diphtheria patients to take the disease.

In dwelling-houses the conditions are not quite the same as in a

hospital, for we have, especially in the poor and lower middle-class, the probability of an insufficient amount of cubic air-space to begin with (it is 2000 cubic feet to each patient in the Metropolitan Asylums Board Hospitals); and the disposal and disinfection of all articles likely to be contaminated are either altogether neglected or inefficiently performed. This will account for such cases as infection from a pillow, from drinking vessels, from toys, picture-books, &c.

It has also been noted that "isolation" in private houses even of good class is in many instances quite perfunctory. The first patient attacked being placed in a room with perhaps good air-space and every attention, recovers; but a second or third, when attacked, is placed in the same room, without it having been previously disinfected; each additional patient diminishing the air-space of the chamber, and contaminating its contents, from ceiling, floor and walls, to every article of furniture, toilet, and food vessels.

In the poorer class of houses, and especially in tenement buildings, this factor of dissemination is enormously magnified, and the greatly increased numbers of this form of habitation may be one of the factors of the greater prevalence of diphtheria in urban districts in the last ten or fifteen years.

As to "**school influence**," it cannot be logically claimed as responsible for the actual origin of the disease, although the frequent following of diphtheria on epidemics of sore-throat or forms of pseudo-diphtheria is undoubted, and may be taken as an illustration of Dr. Thorne Thorne's very reasonable theory of "the progressive power of infectiveness." There is, however, no evidence to show that these epidemic sore-throats take their origin in school aggregation. Indeed, the contrary has been proved by very carefully compiled statistics in a series of able articles from Mr. Biddle, who takes special note of the fact that *mortality from diphtheria is by far the greatest* amongst children under five years of age, that is to say, *within the age limit of compulsory school attendance,* and also that there is a much greater and immediate rise in

diphtheria prevalences in schools on reassembling after holidays than in the middle of a term.—(*Med. Press and Circ.*, Feb. 6, 1895, p. 153).

The experience of all practitioners as to the portion of the term at which these and similar outbreaks are most apt to occur in private schools will agree with this pronouncement.

Mr. Biddle justly "contends that children for the most part incur greater risks at home or in the streets than they do at school, and that if proper care were taken, their attendance at school might be made available for discovering houses that had infectious cases in them, whether diphtheritic or otherwise."—(*Lancet*, Oct. 20, 1895, p. 342).

Further considerations under this heading are rather suggestive of prophylaxis than as germane to causation.

Sporadic, separate, or solitary cases of diphtheria, without obvious exposure to previous infection, are rare. Huebner's explanation that these cases arise through the influence of cold, inducing spasm of the superficial capillaries of the pharynx, to be followed by complete cessation of the circulation and diphtheric exudation, is certainly suggestive; but in such a case the hygienic surroundings of the patient must presumably be favourable for the settling and development of bacterial germs.

As these pages are going through the press, we add the following paragraph from the annual report of Dr. J. C. Thresh, Medical Officer of Health for the Maldon Rural Sanitary Authority for 1894:—"There has been a very marked diminution in the cases of diphtheria notified. In previous years the great majority of those who suffered from diphtheria resided in Heybridge. In 1892, 26 out of 57 cases were reported from that parish; and in 1891, 90 out of 128. Yet out of these 116 cases there was only one death. Whether these were cases of true diphtheria or not" —most probably not—"their occurrence led to many improvements being made in the sanitary surroundings of the dwellings, and it is satisfactory to record that *only a single case* was notified from Heybridge during the past year."

CHAPTER III.

ETIOLOGY—*continued.*

THE BACTERIOLOGY OF DIPHTHERIA AND OF ITS ASSOCIATES.

ALTHOUGH the study of micro-organisms in relation to disease may be said to date from the year 1675, when Leeuwenhoeck gave an account of the larger species of bacteria, which he had found in animal excretions, the modern science of bacteriology is not yet forty years old, and it is less than half that time since the micro-organism of diphtheria was identified. A whole army of observers might be named in the history antecedent to this event, but in the forefront of pioneers in this region of discovery will always stand out the two names of Pasteur in France and Koch in Germany.

It is generally stated that the bacillus of diphtheria was first described by Klebs of Zurich in 1883; but Professors Hamilton and Sternberg have drawn attention to its discovery by the same observer, and to publication of the fact at a Congress held at Wiesbaden, so far back as the year 1875. The circumstance appears to have attracted but little attention, notwithstanding that on examination of the original reference it is found that Klebs had announced at this date that he had not only detected the rod, but that he had also made an effort to cultivate it, and, as far as one can judge, successfully. To Klebs, therefore, the credit of having discovered this organism is undoubtedly due. But since he never definitely announced that he had been able to obtain pure cultures of it, it must be said that he failed in establishing its causal relationship to the disease.

This was effected by Loeffler, who made pure cultures of the bacillus obtained from the throat membrane, and communicated

the disease to guinea-pigs and birds, by inoculating them on the pharynx, larynx, and other parts, with the products so obtained. On all these grounds, with the name of Klebs that of Loeffler will always be associated, because of his commendable and painstaking investigations of the specific taint-quality of the bacillus, and of his reticence in the announcement of his conclusions until he was convinced of their accuracy. This he did in the year 1884.

We will now briefly recount the grounds for Loeffler's belief as to the identity of the bacillus of diphtheria with the causation of the disease, and some interesting corroborative experiments.

I. *It is found in all cases of undoubted diphtheria.*—In 1888 D'Espine demonstrated the presence of the bacillus in 14 cases of characteristic diphtheria, and during subsequent years numerous other observers, including Roux and Yersin, and Von Hoffman, have abundantly confirmed this statement. It has also been demonstrated that it can frequently be found in the throats of convalescent patients.

II. *The bacillus can be found only in cases of undoubted diphtheria.*—D'Espine when demonstrating the presence of the bacillus in the above mentioned 14 cases of true diphtheria, showed further, that it was absent in 24 cases of mild sore throat, which were clinically considered to be diphtheria. This observation has also been definitely confirmed.

Doubts have, however, been recently expressed by Hansemann, Fürst, and others, as to the universal presence of the bacillus in cases of true diphtheria; to which it may be replied, that the proportion of the cases in which the bacillus is not found is no larger than that in which it is found in the mouths of healthy individuals. With more sure methods of bacteriological examination, the number of these is becoming smaller and smaller.

III. *The inoculation of pure cultures induces the disease in animals.*—With regard to this point there was at first some difficulty, for although it was quite easy to produce a malady, with typical throat membrane, yet the fact that false membranes

may be caused by scalding fluids, irritant poisons, or, as in one well known case, by Eau-de-Cologne, rendered the development of membranes an unreliable indication of the disease. The necessary proof, however, was supplied when Roux and Yersin showed that, in a pigeon, paralysis came on three weeks after the pharynx had been inoculated with the bacillus, and when, further, the membrane had quite disappeared, and the bird was to all appearance well.

They also showed that in rabbits the paralysis usually commences in the posterior extremities, and then gradually extends itself over the whole body, causing death by paralysis of the heart or respiratory apparatus. Welch and Abbott confirmed these observations by similar experiments on kittens.

Another argument advanced against the specificity of the bacillus is in regard to exudation in the nostrils. Rarely as is diphtheria confined to the nares—0·2 per cent. in our 1000 cases —there is without doubt a form of *rhinitis fibrinosa* which, although containing the bacillus, is more chronic in its features than when the nasal diphtheria is associated with faucial or laryngeal exudation. The fact that the bacillus of diphtheria is not always to be found in plastic rhinitis only proves that here, as in the fauces, the exudation may be sometimes due to the diphtheria bacillus, and sometimes to the presence of micrococci.

The discovery of the specific bacillus settled what threatened to be an endless controversy as to whether diphtheria is primarily a local or a general disease, in favour of the doctrine that it is in the first instance local. By recognition of its associated organisms we can distinguish the process changes which are caused by the bacillus, from the many complications which are no part of the disease, when exhibited in its pure form. We thus find it possible to separate cases of true diphtheria from the various conditions which clinically resemble it, whereas before the causal relationship of the Klebs-Loeffler bacillus to diphtheria was known, observers were obliged to rely upon clinical features only. Thus, not only our diagnosis and prognosis, but also our measures for

treatment and prophylaxis are now based on a more intelligent and rational foundation.

Virchow and Von Recklinghausen, in their early descriptions, distinguished three varieties of throat disease, in which changes in the mucous membrane occur. These they called *catarrhal*, *fibrinous*, and *diphtheritic*.

Weigert further subdivided the fibrinous form into *croupous* and *pseudo-diphtheritic*. Either of these classifications, now that the bacillary origin of the disease is acknowledged, is open to many objections.

A more useful one, and that here adopted, would be to separate the various forms of membranous sore throat, whether in fauces, nares, or larynx, into **pure** or **simple, impure** or **complex,** and **pseudo** or **false** diphtheria, according to the presence of the bacillus alone, to its presence in association with other bacteria, or to its absence altogether. And lastly, in relation to the existence of the bacillus in a **non-virulent** form, of which more anon.

The final step was to prove that, although death in many cases of diphtheria resulted from mechanical obstruction, yet there remained a large majority in which the fatal result was due to systemic poisoning. This also was settled by Roux and Yersin, who demonstrated that by inoculating animals with the liquid from filtered cultures from which all micro-organisms had been removed, all the diphtherial symptoms could be produced, with the exception of the membrane. These facts were confirmed and emphasised by Fraenkel and Brieger, Sidney Martin, Hankin, and others, and the last link between the etiology of diphtheria and the Klebs-Loeffler bacillus was thus forged.

From the threefold aspect of diagnosis, prognosis, and treatment, the importance of an accurate recognition of the specific organism in any given case of membranous sore throat cannot be better emphasised than by the following figures, furnished by Hermann Biggs :—

From May 4th, 1893, to May 4th, 1894, 5611 cases of suspected diphtheria were subjected to bacteriological examination in the

laboratory of the Health Department of New York city. Sixty per cent. of these cases containing the specific Klebs-Loeffler bacillus were proved to be true diphtheria, while the large proportion of forty per cent., by its absence, were deemed to be false diphtheria.

In a recent account by Drs. Washbourn and Goodall, of 80 cases admitted to an infectious fever hospital, certified to be suffering from diphtheria, only 61 cases were found to contain the bacillus. In 19 cases in which the bacillus was not found, 8 would not have been considered as diphtheria, even had not a bacteriological examination been made; on the other hand, there were 11 non-diphtheric cases which were on clinical grounds diagnosed as diphtheria; in all these the further progress of the cases fully bore out the bacteriological evidence of their non-specificity.

In other words, an error in clinical diagnosis was made to the extent of 23·75 per cent. of the whole 80 cases. Ten per cent. of these were corrected on admission by the Medical Superintendent of the Hospital, and of the remaining 61 cases admitted as true diphtheria, 18 per cent.—13·5 of the whole 80—received correction only after bacteriological examination.[1]

A third observation is that of Chaillon and Martin, who classify 99 cases of faucial angina, bacteriologically examined, as follows:—

Pseudo-diphtheria (bacillus absent), .	29,	with no	deaths.
Pure diphtheria (bacillus only), . .	44,	„ 10	„
Complex diphtheria (bacillus with cocci), or diphtheria with associations, . .	26,	„ 18	„

[1] It is only fair to state that the proportion of corrections in the clinical diagnosis by bacteriological examination varies at the different infectious fever hospitals of the same class. Thus at one, "of 61 cases all clinically diphtheria, the diphtheria bacillus was found in 55 [*Lancet*, Feb. 2nd, 1895, p. 305], a difference of 8 per cent." In another, of 45 consecutive cases, "44 were certified by bacteriological examination to be true diphtheria," a mistaken diagnosis of only 2·2 per cent. [*Medical Press and Circular* Feb. 13th, 1895, p. 159.]

The Klebs-Loeffler Bacillus.

This, the specific micro-organism of diphtheria, is a minute straight or slightly curved rod, measuring from 1½ to 2 or 3 micro-millimetres in length, and 0·5 to 0·8 in thickness—that is to say, slightly longer but much broader than the bacillus of tubercle. The organisms occur either singly or in pairs (Fig. 2), frequently more or less parallel to each other (Fig. 3), or at an obtuse angle, like a circumflex accent, seldom end to end, and sometimes in small groups of three or four, often arranged fantastically, so as to bear close resemblance to letters of the alphabet, as V, M, N, X, Y, &c., or every variety of cuneiform character (Fig. 4); finally, the bacilli are sometimes, though rarely, arranged in chains (Fig. 4). Their outlines are not uniformly cylindrical, for a bulging is often seen at the ends. They show a characteristic segmentation of from two to five elements of protoplasm, and they stain in a peculiar way, one or other pole, often both, and sometimes patches of protoplasm between the poles being more deeply stained than the rest. The bacilli are said not to contain spores, but highly refracting particles may often be seen between the more deeply stained portions.

Another reputed characteristic of these bacilli is that an appearance is occasionally witnessed (Fig. 5) as if the protoplasm was shrinking away from the cell-wall, leaving a more or less regularly uncoloured or but lightly coloured space at the periphery.

Three varieties of the bacilli are recognised according to their microscopical characters, namely, the **long**, the **short**, and the **medium**; they are also variously described according to their diameter as **thick** and **thin**. Their differences in length and calibre probably represent various stages or varying richness in the growth, for at present definite evidence is wanting to show that variations in the size of the bacilli, either in length or thickness, represent differences in the degree of their virulence. The tendency is towards attributing greater virulence to the long

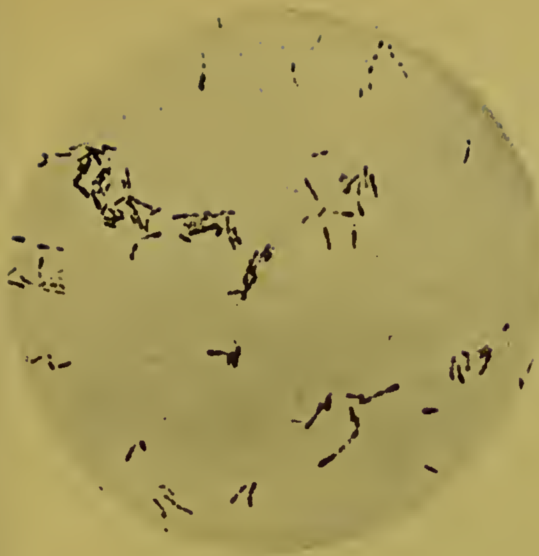

Fig. 2.

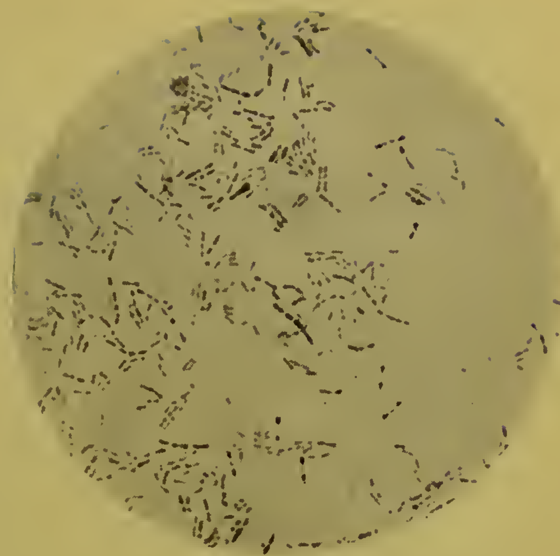

Fig. 3.

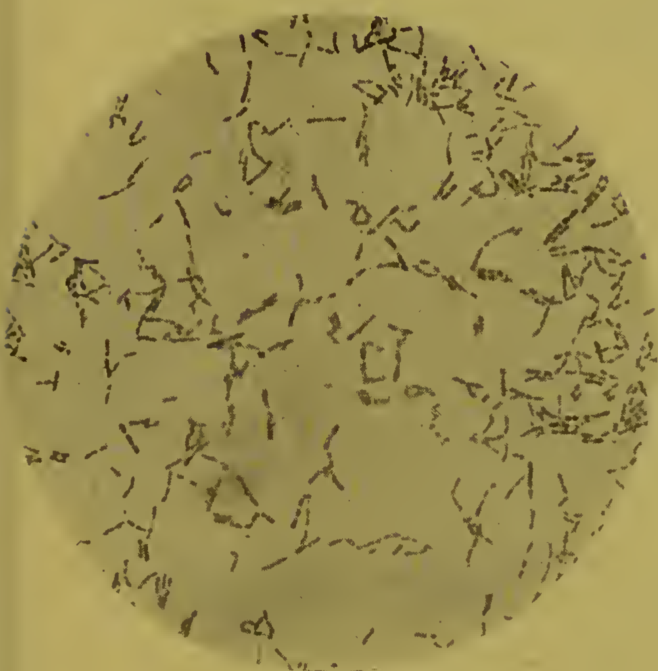

Fig. 4.

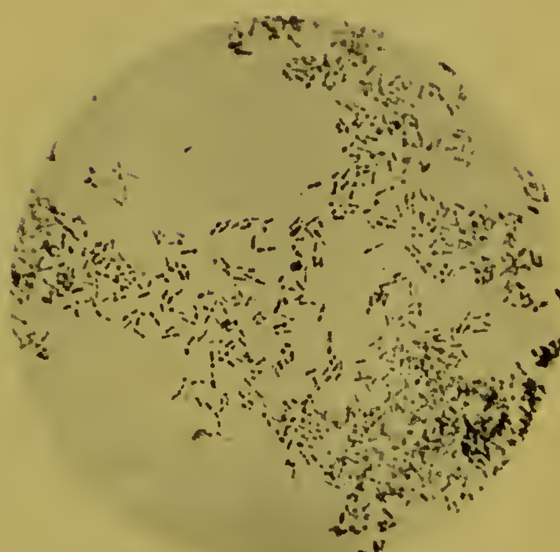

Fig. 5.

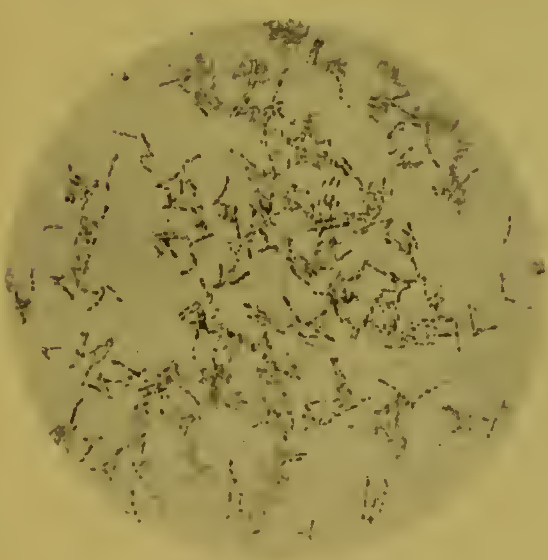

Fig. 6.

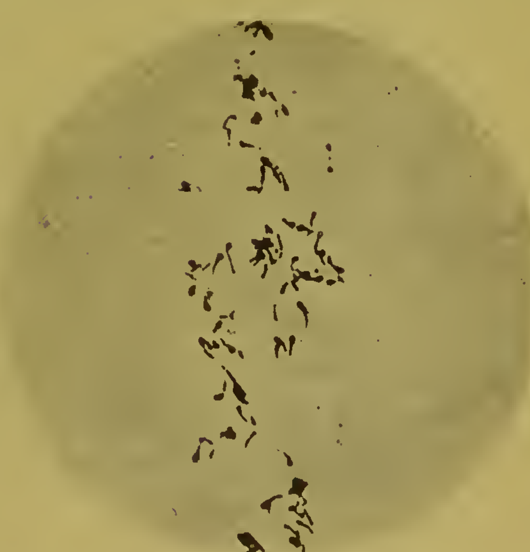

Fig. 7.

The Bacillus Diphtheriæ.

variety, since the bacilli examined during convalescence are almost invariably of the shorter kind.

But the size of the bacilli, and also their method of staining, would appear to depend somewhat on the medium in which they are cultivated, cultures on glycerine-agar developing less fully and staining less characteristically than those grown on blood-serum.

Fig. 7, representing a culture on milk from a specimen by Professor Klein, illustrates a still more striking difference in form, so different, indeed, that it would be well, if agreement were more general, to publish only cultures made on one particular medium. Of these, for all purposes of education and comparison, blood-serum is undoubtedly the best.

Associated Micro-Organisms.

The micro-organisms of clinical importance as associates of the diphtheria bacillus are mainly cocci. Of these we have—

(1) Those arranged in pairs—diplococci.
(2) ,, ,, groups—staphylococci.
(3) ,, ,, chains—streptococci.

As to the **diplococcus**, which is seen in the illustrations to be associated with streptococci (Figs. 8 and 9), it is sufficient to say that it is usually identified with the organism supposed, when encapsuled, to be specific of pneumonia. However, not only free diplococci, but those encapsuled, are to be found in membranous sore throats, and even in healthy ones, unaccompanied by pneumonia, and in other diseases than pneumonia. The evidence at present is—to say the least—insufficient to support belief in the existence of a pseudo-diphtheria of a high grade, which is characterised solely by the presence of this organism. Our individual experience is, however, that throats in which diplococci are predominant, or are associated with other micro-organisms of greater importance, are "dirty" in character, and slow to clear away of pseudo-membrane.

Some importanee has been attaehed to a eoeeus deseribed by Louis Martin, a eolleague of Roux, and ealled by him, as must be admitted somewhat unseientifieally, "**Brisou,**" after the name of the ehild in whom it was first "diseovered."

Martin names it as forming one of the eolonies whieh have resemblanee to those of diphtheria, and he states that, in the case of the ehild in whom he first witnessed it, the elinieal features so singularly eonfused the diagnosis that the little patient was taken seven times to the diphtheria ward for a diphtheria whieh he had not.

The points of distinetion on eulture will be eonsidered later,

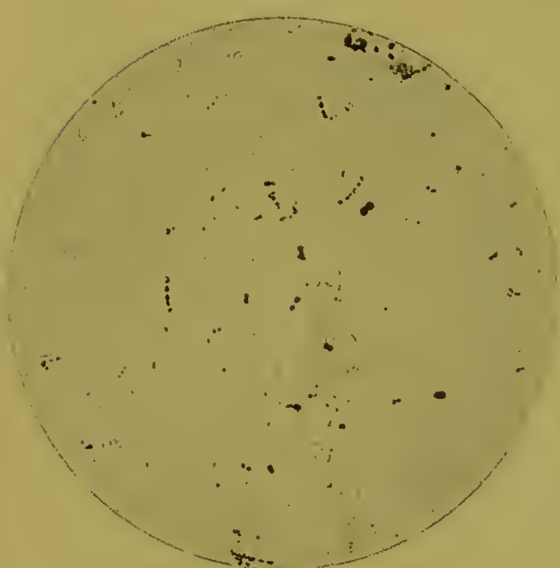

FIG. 8.

FIG. 9.

DIPLOCOCCI with STREPTOCOCCI RIGIDI.

and it is suffieient here to refer to its mieroseopie features, whieh, as Martin says, should remove all doubts. He deseribes the appearanee of this eoeeus as little points isolated or grouped two by two, but as the figure (No. 10) shows, they may oeeur in eombinations of 3, 5, 7, or even 10.

These eoeei will be notieed in some of our own photo-mierographs, and in them, as in Martin's illustration, they would appear to represent, to the ordinary eye, organisms hitherto considered as without importanee and identieal with those whieh are so

frequently present in specimens of secretion from the upper respiratory passages and in pulmonary sputa, while the larger groups are almost indistinguishable from small heaps of staphyloeoeci. One is, therefore, somewhat at a loss to know why so much prominence has been given to so common and innocuous an organism, and it is to be hoped that a lead, which has already been given in this country, to attach to it clinical importance will not be followed.

Staphylococci, *Albus*, *Citreus*, and *Aureus*, and mainly the latter, in eases of membranous sore throat, are generally associated with strepto- or diploeocci, but in eertain eases, especially those attended

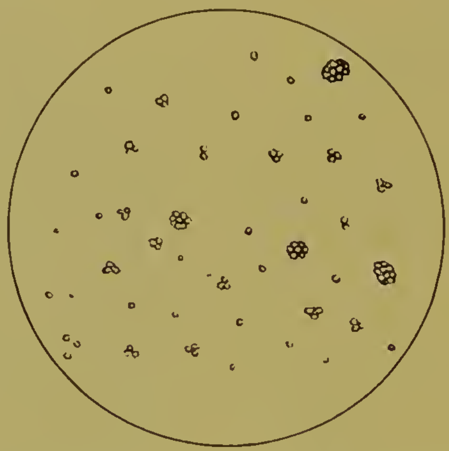

FIG. 10.—"BRISOU" COCCUS. (*Facsimile*, after Martin.)

by suppuration, they may represent the only micro-organism present. Instances are to be seen in Fig. 11, and also in assoeiation with the bacillus and streptococci in Fig. 12. Fraenkel speaks of another staphylococcus which does not liquefy gelatine.

Streptococci, when alone, generally represent a membranous sore throat assoeiated with the exanthemata, of which scarlet fever is the most usual, for this organism is almost invariably to be found in the throats of scarlatinal patients; not that we mean to imply that this eoecus is the specifie miero-organism of scarlet fever, for that at present is undiscovered; but when found associated with the bacillus of diphtheria it is an almost

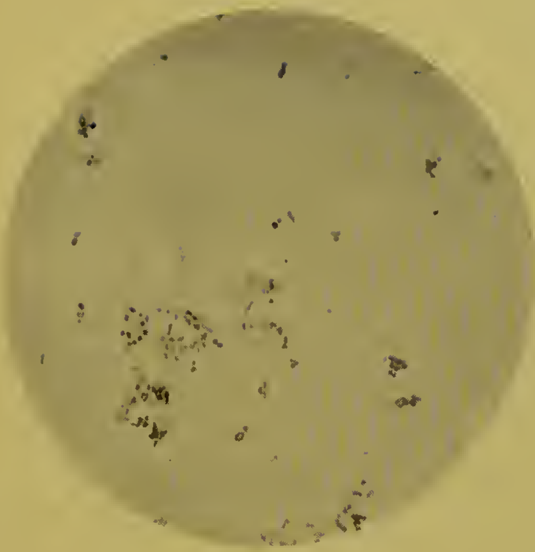

Fig. 11.

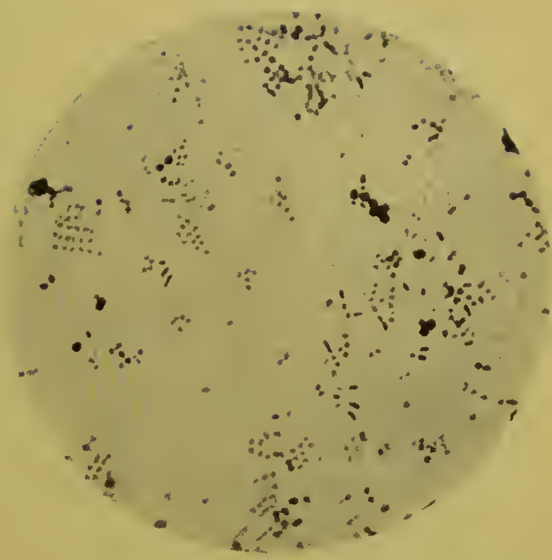

Fig. 12.

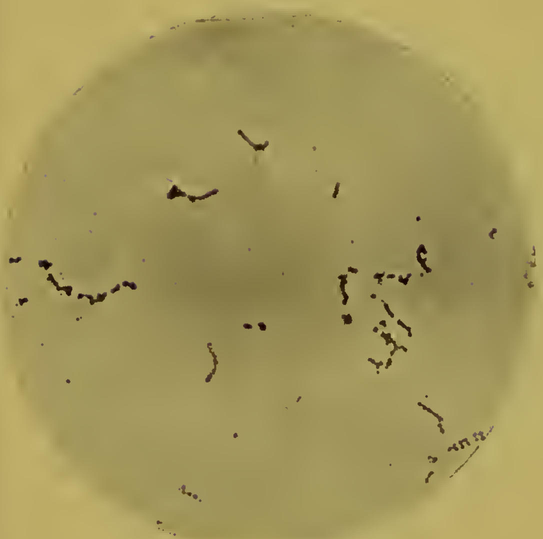

Fig. 13.

Fig. 14.

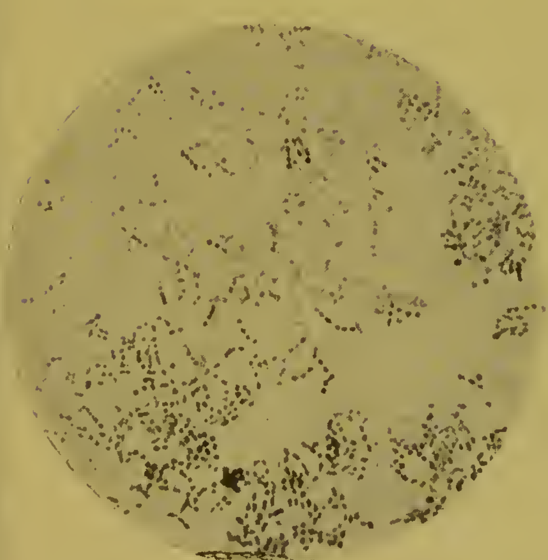

Fig. 15.

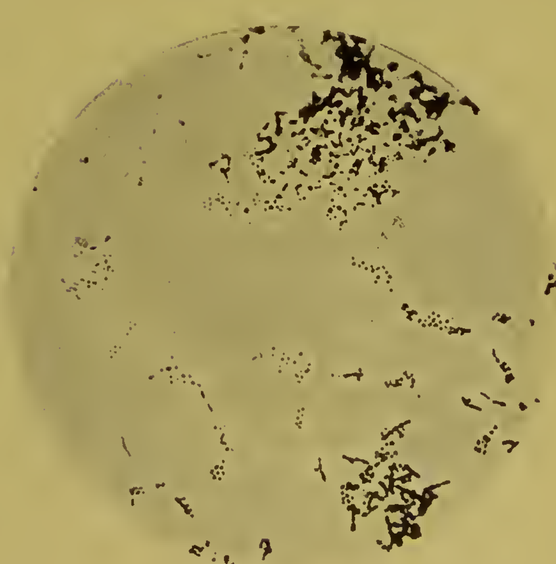

Fig. 16.

unerring indication for grave prognosis, and represents an attack of diphtheria which has probably supervened on one or other of the acute specific fevers, probably scarlet fever or measles.

Kurth was the first to point out that the arrangement of the streptococci bears some relation to their virulence, but the importance of this fact has been very generally overlooked, both in this country and in France.

First in simplicity of order and mildness of indication are the *Rigid*, in which the chains are short and straight, as in Figs. 8 and 9, which represents the arrangement found in a case of insanitary tonsillitis.

Next in severity are the *Flexuous*, in which the chains are curved or coiled, as notably exemplified in Figs. 13 and 14, which were both taken from a case of pseudo-diphtheria occurring during scarlet fever.

Lastly comes the third form, *Conglomerate*, or, as we have ventured to term it, the *Batallion* arrangement, in which the chains are grouped in serried ranks, sometimes in parallelograms, sometimes in triangles, or in simple double file, one rank being longer than the next by one or more elements. These are found in the most virulent forms of complex diphtheria—namely, those which are implanted on a scarlatinal or rubeolar pseudo-diphtheria, and of which examples are to be seen in Figs. 12, 15, and 16. In Fig. 14 all three varieties are shown in the one slide. The illustration is from a drawing, not a photo-micrograph.

Independently of these coccal organisms and of the specific bacilli, others are found. There is one which bears a strong resemblance to the **bacillus coli**, and many unnamed and without significance. Lastly, it should be mentioned that, in some of the milder forms of throat inflammations allied to diphtheria, such, for example, as insanitary tonsillitis and non-bacillary lacunar inflammations, a **mycelium** may be present. Plant has recorded that, in some cases of non-diphtherial angina, he has found **Miller's spirochœta**.

The "Pseudo-Diphtheria" Bacillus.

Suggested Synonym.—The **attenuated** or **non-virulent** bacillus. We have reserved to the last the consideration of a bacillus difficult to distinguish from the genuine organism of diphtheria for in its method of growth, the formation of its colonies, and its microscopical appearance it is absolutely identical with the Klebs-Loeffler. Nor does it readily lose any of these characteristics on further cultivation.

The likeness of the two microbes consists not only in the appear-

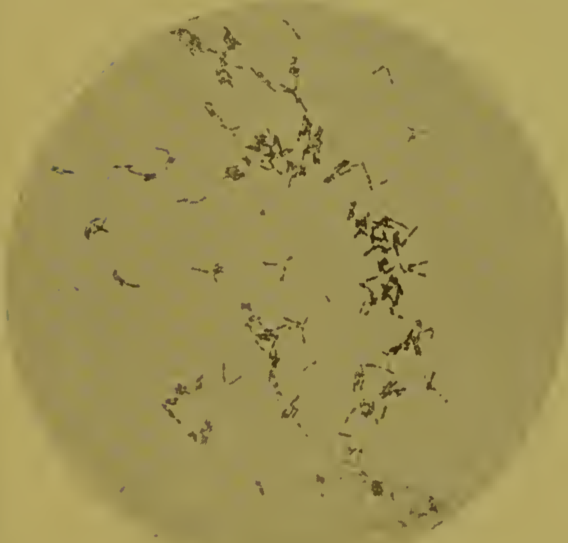

Fig. 17.

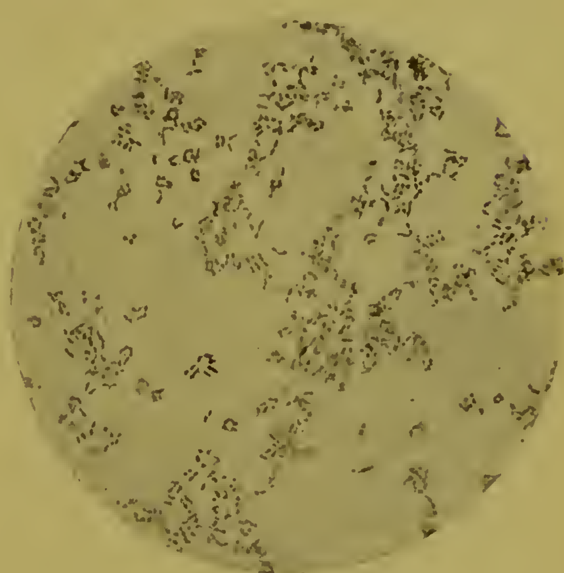

Fig. 18.

ance of the bacilli separately, but in that fantastic alphabet arrangement, to which allusion has been made as a special feature in the identification of the true organism. Appended (Fig. 17) is a photo-micrograph of a beautiful example of this "pseudo-diphtheria" bacillus, as it has, in these days of exactitude, been somewhat unfortunately named. The preparation was given to me by my young friend, Dr. Taylor Grant, who obtained it from a specimen of diphtherial membrane, afforded from the laboratory of Dr. Roux. The specimen represents a pure culture, but the original contained a few staphylococci. If one compares it with others of admitted

virulence, it is impossible to detect any real difference either in form or arrangement; and any bacteriologist obtaining such a result would not hesitate to give an opinion as to the true diphtherial character of the case from which it was taken. In point of fact, the only method of distinguishing this "pseudo-diphtheria bacillus" from that of the veritable Klebs-Loeffler organism is by an experimental observation of its non-toxic effects when introduced into the bodies of rabbits or guinea-pigs, that is to say, that although so similar in form, and responsible even to produce a membranous inflammation of the throat, it is **non-virulent** in the sense that it is incapable of producing toxæmia either in the person of the individual in whom it is found or by inoculation of lower animals. But such a protracted investigation as would establish this negative property is clearly quite impossible in ordinary practice, and a doubt must therefore naturally arise, in the light of the after history of at least some of the cases which, as the result of a bacteriological examination, have been declared to be true diphtheria, whether the specific organism has really not been of this benign character.

For example, the case from which the Figure 4 was taken, that might be placed in comparison with that of the "pseudo" bacillus, was diagnosed by me to be one of lacunar tonsillitis, probably of insanitary origin. For the notes of this case, and the details of the appearances of the fauces on the occasion of first inspection and that presented two days later, which appeared to justify this view, the reader is referred to *Case* 4, Chapter VIII. And since this patient made a rapid and complete recovery—without any paralytic sequelæ—there must still remain a doubt whether the diagnosis made at the bedside or that emanating from the bacteriological laboratory was correct. By a coincidence, since these words were written, this patient has again come under my care for the purpose of having his tonsils removed.

Two days after the operation a curious exudation appeared on the wounded surfaces, which, on bacteriological examination, both by culture and microscope, exhibited all the characteristics

of the pseudo-bacillus, as will be ascertained by the following report:—

"Two cultures were made in this case, one from membrane sent in a culture tube, the other from membrane adhering to the swab. The cultures obtained were both of the same character, large, isolated, greyish white colonies, about twenty on the swab culture, about twelve in number on the other.

"On microscopic examination bacilli of similar characters were obtained from each culture, accompanied by staphylococci. The bacilli were short and segmented, many being club-shaped and showing the character of the short variety of the bacillus diphtheriae. They are somewhat shorter than specimens of the Klebs-Loeffler bacillus usually obtained, and may be the pseudo-bacillus of Roux and Yersin" (Fig. 18).

A subculture showed colonies still more sparse and consisting mainly of cocci; a further subculture failed to produce any development of the bacillus, the whole growth consisting of cocci. It is, therefore, to be presumed that in this case active cocci destroyed the attenuated bacilli.

Dr. Sims Woodhead and other observers tell me that this particular specimen exhibits just the changes they are in the habit of witnessing in the examination of secretions of convalescent patients.

Judgment as to the category under which this "pseudo-diphtheria" bacillus should be classed is rendered all the more uncertain by the affirmed differences of opinion which exists among eminent observers in regard to the question whether it can or cannot be re-stimulated into virulence.

All these circumstances tend to show that an error in clinical diagnosis cannot always be corrected by bacteriological methods, either so easily or so speedily as has been pronounced, and that the cases in which this difficulty may arise are precisely those in which a mistake by the clinician of experience would be most probable.

Naturally, the worker in the laboratory is not satisfied unless

he can prove everything to a mathematical conclusion, but we, as clinicians, may be permitted to view this and several other bacteriological questions, at present undecided, by the light of common sense. Thus it appears only reasonable that as the specific organism of diphtheria is to be found on the floors, ceilings, walls, and furniture of rooms, through which many persons pass without infection, so also the organisms may be present in some throats which are non-receptive, or in those individuals who are possessed of sufficient powers of resistance to either greatly modify or annihilate them.

We also learn that no two horses are alike in their power of resistance to the action to the toxine of diphtheria when undergoing inoculation for the purpose of immunisation. If, then, there is this variability of resistance in the man and the horse, why not — at any rate occasionally — in the rabbit or guinea-pig, the effects of experiments on which constitute the basis of argument?

We are told that the virulence of the true bacillus decreases at the end of a few weeks or months, and in process of time entirely disappears. Introduction of fresh bacilli into an attenuated culture will bring about a recrudescence of its toxic properties. If this can be effected in the laboratory we may understand the position which the so-called pseudo-bacillus holds in the estimation of various observers, one set believing it to be capable of regaining its toxic power, and the other that once innocuous it is incapable of ever again inflicting injury.

As a corollary of Dr. Thorne Thorne's theory of progressive development of infectiveness in the waxing of an epidemic, not only of diphtheria, but of other infectious diseases, it is within experience that there is a decrease in virulence as it wanes. It is suggested that it is in this aspect that the non-virulent bacillus is to be regarded, and it would be desirable before confusion has become more widely disseminated, that it should be renamed by some term which would definitely express its attenuated properties.

Unless some such broad view, as is here suggested, be taken of this question, it would not be difficult to convert the "pseudo-bacillus" into a very Frankenstein, which would speedily destroy acceptance of the bacillary origin of diphtheria, as at present recognised.

CHAPTER IV.

ETIOLOGY—*continued.*

THE TOXIC PRODUCTS OF THE DIPHTHERIA BACILLUS AND ITS ASSOCIATES.

THE causal relation of the specific bacillus of diphtheria to the disease having been established, it still remained a moot point to what extent the manifestations of the malady could be attributed to the presence of the organism in the membrane until 1889, in which year all doubt was cleared up by experiments which scientifically determined the process, and established the fact that all the symptoms of diphtheria, except that of the development of membrane locally, are caused by the action of a definite poison.

Chief among the workers in this interesting field of research are Roux and Yersin, Hankin, Brieger and Fraenkel, Sidney Martin, and Klein, and this chapter will be devoted to relating as succinctly as possible the various conclusions at which these and other authors have arrived.

Before proceeding further, however, the writer may be excused for recalling the circumstance that, in the interval between the discovery of the bacillus and that of its power to produce toxines, he had in 1887, on clinical grounds alone, ventured to promulgate the view, which was at the time adversely criticised, that the principal cause of death in diphtheria was a poisoning of the system by fermentative products of the special organism, expressing the opinion, in the second edition of his book, in the following words :—

"The tendency in this country at the present day, especially amongst younger and more advanced pathologists, is to accept

provisionally the notion that diphtheria is at first a local disease, associated with the growth of micro-organisms on some mucous membrane or abraded spot. During the course of an epidemic it is supposed that spores enter, say, the mouth of an individual, and either do or do not find in the oral secretions of such individual, after being challenged by the scavenging leucocytes, a suitable culture medium. If the nidus be a favourable one the microbes germinate on the mucous membrane of, for example, some part of the pharynx or fauces; as reproduction proceeds apace, the multiplied organisms in the course of from two to eight days pass into the tissues; and this invasion soon results in those pathological changes so characteristic of diphtheria, the false membrane. The life processes of the multiplying microbes are accompanied by fermentative changes, and the production of poisonous albumins and ptomaines, which pass into and contaminate the blood: systemic poisoning is thus accounted for."

Of course I was in error in supposing that the specific poisons were ptomaines, but the suggestion to that effect was in accordance with the views then held, that all bacterial poisons were alkaloidal in their nature. Since then this specific property of such products has been definitely disproved.

The following is the method employed by Roux and Yersin, who were the first to successfully obtain the toxines.

The original broth culture of the bacillus is carefully filtered through porcelain to eliminate the microbes, and the filtrate is then precipitated by alcohol, dissolved in distilled water, and again extracted with pure alcohol; the precipitate being dried *in vacuo*.

By this process is obtained a white, or as some say, a yellowish powder, which is soluble in water. It is almost always neutral in reaction, but sometimes faintly acid.

The powder is able to induce all the symptoms of diphtheria, except the membrane; but its toxic potency is very much reduced by exposure to a comparatively low temperature—58° C. for two hours—and is completely destroyed by the boiling temperature—

100° C. for twenty minutes. The same effect is produced if the powder be long exposed to sunlight.

The virulent bacillus renders its culture media acid in 24 to 48 hours; the toxine, however, is only found in alkaline media, and is probably only soluble in alkalies. A free supply of oxygen has been found to promote the growth of the bacilli, to lead to early elaboration of the toxine, and to increase its virulence. The action of the oxygen prevents the media from becoming acid, and Ruffer has noticed that cultures freely exposed to air remain alkaline.

Roux and Yersin found further, that the bacilli, when inoculated into guinea-pigs, continued to multiply for from six to eight hours; but that the animals frequently died, after the bacilli had either very much diminished in number, or had even quite disappeared. They kept cultures for five months, after which they found that although the bacilli were not so virulent as when the cultures were fresh, they were still fatal to the life of susceptible animals when introduced into them by inoculation. When the virulence of a culture has once been lost it cannot be regained, but if only weakened it can be re-stimulated into activity. Until recently it was held that the power of the toxine depends on the virulence of the bacilli, but this view has lately been disproved. Ruault, for example, mentions that the toxic potency can be increased by the streptococcus of erysipelas, while Roux, Chaillou, and Martin have all drawn attention to the increased gravity of diphtheria when associated with either streptococci or staphylococci; the author's personal experience is in accordance with their conclusions. For, granted that in regard to these associated organisms, a large number are indifferent, and are simple witnesses, not playing any active *rôle* in the evolution of the disease, yet some are truly pathogenic, and appear to be capable of modifying the attack in variable degrees; it may be in augmenting the virulence of the bacillus with which they are associated; it may be in determining the secondary infections, which are superadded to the diphtherial intoxication; or perhaps in both these

directions. Or it may indeed be possible that the diphtheria bacillus itself is capable of increasing the virulence of some of these micro-organisms, ordinarily inoffensive. Lastly, it may be permitted to suppose that certain micro-organisms may exist, which, if present in the throat at the same time as the bacillus, may be capable of attenuating its virulence, or of being attenuated by it.

What is the exact chemical composition of this deadly poison remains at present undecided.

According to Roux and Yersin the toxine of diphtheria is of the nature of a **diastase**, and they give the following reasons for their opinion:—

(1) It comports itself as to heat in the same way as a diastase; that is to say, its power is gradually impaired, and finally destroyed above a certain temperature. Thus, although $\frac{1}{8}$ c.c. of a toxine solution is sufficient to kill a guinea-pig, 1 c.c. of the same solution, when heated for twelve hours at a temperature of 58° C., does not cause death in another of the same weight; not that this dose is absolutely innocuous, for it is capable of killing small birds and setting up œdema in a guinea-pig at the site of injection. In the case of rabbits $\frac{1}{2}$ c.c. is fatal, but after heating for twenty minutes to a temperature of 100° C., the solution is quite harmless.

(2) Like diastase, the toxine loses its toxic properties by the action of air, and by exposure to sunlight.

(3) It is soluble in water, and insoluble in alcohol, the agent employed for its precipitation.

(4) It has the same property as the diastases possess of adhering to precipitates.

(5) Like diastases, the diphtheria toxine loses much of its activity if the medium is made acid.

(6) Its energetic action in infinitesimal doses.

Opposed to this view it has been urged that diphtheria toxine does not invert cane-sugar, or convert starch into glucose, nor does it convert albuminoids into peptones. These criticisms demon-

strate that the analogies of the diphtheria toxine with diastases are lacking in some important points.

Fraenkel and Brieger believe the poison to be a **tox-albumin**, a view that was first promulgated by Hankin, but Wassermann and Prosskauer say that this tox-albumin is a mixture of the albumoses of the bouillon with the true toxine which, as noted by Roux and Yersin, has such a strong tendency to adhere to precipitates.

Thoinot and Masselin have also pointed out that the product obtained by Roux and Yersin is 100 times more toxic than the tox-albumin of Fraenkel and Brieger. Kanthack thinks the name *tox-albumin* is not a good one, because the albuminous or proteid matter can be removed from the poison, and he suggests that the products should rather be called **toxines** or **tox-albuminoids**.

Until recently it was generally agreed by the majority of observers that the field of the bacillus of diphtheria is limited to the superficial parts of the membrane, and that the organism does not pass into the body; for even when injected subcutaneously its development is confined to the site of inoculation. But Bulloch and Schmorl have found the Klebs-Loeffler microbe in the lymphatic glands—submaxillary, bronchial, and mesenteric—and even in the lymphatics themselves, in thirteen out of a total number of eighteen necropsies on children dead from diphtheria. In order to meet the objection that its presence in these situations might be considered to be a *post-mortem* occurrence, all the autopsies were made within five hours after death. Nevertheless, neither this circumstance nor the very rare occasions in which the bacillus has been found in distant organs can be held to weaken the fact that *the Klebs-Loeffler organism is the specific source of the disease.*

That which has been proved to be effected by analysis in the laboratory and by experiments on animals, is probably what takes place during the course of the disease in the human subject.

According to Sidney Martin, the microbe liberates a **ferment** or

enzyme which is readily absorbed, and by its action on the proteids of the body, produces two poisonous substances, namely, *albumoses* and an *organic acid*, which are responsible by their action on the nervous system for all the constitutional symptoms—the fever, the cardio-respiratory asthenia, albuminuria, and paralyses.

Many cases have been recorded of persons dying from the malady whose bodies were found, on *post-mortem* examination, to contain large quantities of the specific toxines; albeit in a considerable number of them, only a very small quantity of membrane had been present during life. Whence it is deduced that the source of all this poisonous material cannot be in the membrane itself, but that it is elaborated in the systems of those affected. This is rendered the more probable by the fact that large quantities of the poisons are found in such cases in the spleen.

Chemical examination of the membrane, even in an early stage of its formation, proves it to be in course of digestion. It is also found to contain a poison which can produce results identical with those obtained from extracts of the blood and spleen of diphtheria patients when injected into animals; but with this great difference that the poison is of a much more active and virulent character when derived from the membrane direct.

The extract thus obtained, however, contains only minute quantities of the albumoses, and the rapidity of its fatal action is due probably to the *enzyme* which has been already mentioned as a product of the bacillus.

Instances—unhappily too common—occur in practice, of rapidly fatal results, of which a satisfactory explanation can only be afforded by acceptance of the foregoing facts.

The false membrane in diphtheria is one of the first results of the specific action of the bacillus. Being composed of fibrin, and moreover being in process of digestion, it constitutes a favourable medium for the growth and multiplication of the micro-organisms.

Sternberg has noted that although a large number of pathogenic organisms are killed by exposure for ten minutes to a temperature

of 55° to 60° C., this comparatively low temperature has probably no destructive effect on any of the poisonous chemical products, which might be supposed to be the cause of infective virulence.

Klein has recently gone a step further, and pointed out that "a definite distinction is to be drawn between the poisons which may be present in the bacteria themselves, and the poisonous substances liberated or elaborated by these organisms." For he has shown that when certain micro-organisms are injected into the peritoneal cavities of rodents, they produce symptoms of poisoning without any of their metabolic products being present. Moreover, if the microbes, previous to their injection, are killed by heat at a temperature of 70° C., these dead bacteria in certain cases produce the same poisonous effects as the living organisms. Therefore, according to Klein, these micro-organisms must contain a poison in their own substance.

The Action of the Toxines.

The Albumoses.—When these products of the bacillary ferment are introduced into the animal body, they produce a local œdema, which subsides at the end of 36 hours, and is not followed by any destruction in the tissues, although some irregularity in temperature, and in the case of rabbits, distinct febrile conditions are found to follow the injection; the blood becomes darkened and more fluid, and its coagulation is retarded.

Larger doses produce a fatal result from **paralysis** or **coma**, but it is worthy of notice that equally noxious, but less rapidly fatal, results are obtained from small doses of the poison frequently administered.

The paralysis may at its onset be rapidly fatal in its effects, or its progress may be slow and protracted; in any case, it is always progressive. The hindrance to the coagulation of the blood offers a suggestive explanation of the delayed occurrence of the paralytic sequelæ of diphtheria, even after all other symptoms of the disease have disappeared.

The paralysis is manifested primarily and chiefly on the cardio-respiratory apparatus. The heart muscle is in all cases in an advanced degree of fatty degeneration. Sidney Martin has "not found any degeneration in the vagus nerve," and he suggests that the muscular degeneration may possibly depend on the altered condition of the blood, or, indeed, that the diphtheria albumoses may have a special action on the heart itself.

Vincent of Paris and P. Meyer have found wide-spread parenchymatous changes in the cardiac plexus in two cases of patients dying of heart failure during convalescence from diphtheria, in which the heart muscle was unaffected. The changes were exactly similiar to those found in the peripheral nerves in ordinary post-diphtherial paralysis. It is desirable that future observations should be directed to the further elucidation of this point.

The voluntary muscles of the body are not by any means necessarily affected at the same time, those first impaired being those which of necessity are in constant use. In all cases impairment of activity of voluntary muscles is due to a degeneration of their nerve supply.

Although there may be at first no apparent atrophy of the muscles, yet the body-weight of the animal decreases steadily.

In diphtheric paralysis both the sensory and motor nerves are affected in a similar way, and the sympathetic system may be also involved, but, as would be expected, the part most affected in this case is the axis cylinder.

The central nerve cells and ganglia in the spinal cord are most probably not the original site of the lesions which take place in the nerve trunks, for although morbid changes have been described by some pathologists in the anterior cornua of the cord, none have been discovered in those of the posterior cornua or sensory ganglia, albeit both the motor and sensory nerves share in the degenerative process.

The affection of the nerves must therefore be regarded as being entirely of a peripheral nature.

The change commences in the white substance of Schwann,

which undergoes rapid degeneration, breaking up and finally disappearing altogether. Following on this the axis cylinder may become ruptured — **Segmental Neuritis** — giving rise to well-marked Wallerian degeneration in the nerve fibres below the point of rupture. All the nerve fibres, however, may not be affected to the same extent, and some may still retain their power of conveying nervous stimuli to the muscles which they innervate.

The muscles which are deprived of nervous supply by the rupture of the axis cylinders in the nerve-trunks undergo a process of fatty degeneration and atrophy.

The albumoses in diphtheria are therefore to be regarded as nerve poisons, which affect the peripheral nerves, and if administered in small and continued doses produce degeneration of the nerves, leading to both paralysis of motion and sensation.

It is to be borne in mind that these paralyses may occur early in the acute stages of the disease, or in the later when they come under the head of sequelæ.

The Organic Acid. — This, the secondary bacillary poison, when injected into animals, produces fever to a slight extent, but no paralysis. If, however, an animal be treated with several doses at intervals, the heart *post-mortem* shows well-marked fatty degeneration in the muscular elements, and some of the nerve fibres exhibit stages of degeneration similar to, but of a less degree than, that produced by very small doses of the albumoses. From these observations the organic acid must be regarded as a nerve poison of a much weaker nature than the albumoses.

The presence of **Associated Cocci** is responsible for modifications in the degree of virulence of the diphtherial toxines; this is especially manifested in the difference in the character of the cardiac, pulmonary, renal, and other lesions. In point of fact, an infective process, due to the cocci, is superadded to the specific intoxication of the diphtherial poison.

CHAPTER V.

PATHOLOGY.

MORBID ANATOMY OF DIPHTHERIA AND ITS ASSOCIATES.

DIPHTHERIA has been known under numerous names, such as Syriac Ulcer, Egyptian Throat, Garotillo, and other equally indistinctive terms, some of which have been mentioned in our brief history of the disease. It can hardly be said that the modern term is much better than those previously used.

As is well known, the word Diphtheria originated with Bretonneau, who termed it **diphtheritis**, to represent an inflammatory disease of the throat, characterised by an exudation possessing the appearance of skin, parchment, or leather; though he was by no means the first to draw attention to this peculiar macroscopic feature, and as has since been shown it is one that is by no means constant. Trousseau, justly recognising that the inflammatory process of pure diphtheria is not of a high grade, suggested the term *diphthéric,* whence we get the word **diphtheria**. It is now known that from time to time cases are seen in which the exudation may be represented by the thinnest pellicles of deposit, and that false membrane may indeed be altogether absent, with no diminution of virulence or regularity of sequence of all the characteristic symptoms. The term **Diphtheria** is now accepted as representing a disease of which the pathognomonic and unalterable characteristic is the presence of the specific bacillus known as the Klebs-Loeffler.

It is rather difficult in treating diphtheria in the practical manner at which this treatise aims, to satisfactorily consider all the various elements of its pathology under one chapter; and it

has therefore appeared preferable to assign so much of it as relates to the bacteriological question to the special chapters on Etiology, and to relegate to that section which will embrace the Elements of Prognosis, consideration of those morbid changes which, occurring during the ordinary course of the disease or as complications and sequelæ, can be diagnosed at the bedside and verified, it may be, on necropsy.

Comparatively brief space will therefore be required for an account of the morbid anatomy which remains to be considered; but without trespassing unduly on the proposed plan, there may be mentioned, in addition to those changes witnessed in the throat and air-passages, certain others to be detected on *post-mortem* examination of every subject dying from diphtheria.

Thus, whatever the immediate cause of death, there is, independently of the localities which are the sites of the exudation, a *general congestion* of the whole extent of the *respiratory tract.*

The same applies to the *digestive tract.* The intestinal mucous membrane is generally hyperæmic, and—according to Rnault—there is marked hypertrophy of Peyer's patches in about half the cases.

The *spleen* and *liver* are congested and enlarged, the latter often showing evidence of fatty degeneration.

Equally there is *general vascular dilatation,* with inflammation of the *lymphatic glands,* and sometimes *abscesses.*

Albeit the *heart* may appear healthy, the muscular fibres will, in almost every case, be found to have undergone more or less fatty degeneration.

The *kidneys* especially partake in the general congestion.

Whether all these changes are due to the toxic action of the diphtheria bacillus, or to that of superadded micro-organisms, these several lesions need not at present be further discussed. It is here sufficient to record them.

The **diphtherial membrane** being indubitably the primary pathogenic offspring of the bacillus, calls for more special attention.

The microscopic structure of diphtherial membrane is well shown in the excellent plate, for which we are indebted

to Professor Hamilton. The exudation is poured out on to the surface of the mucous membrane, and, being rich in

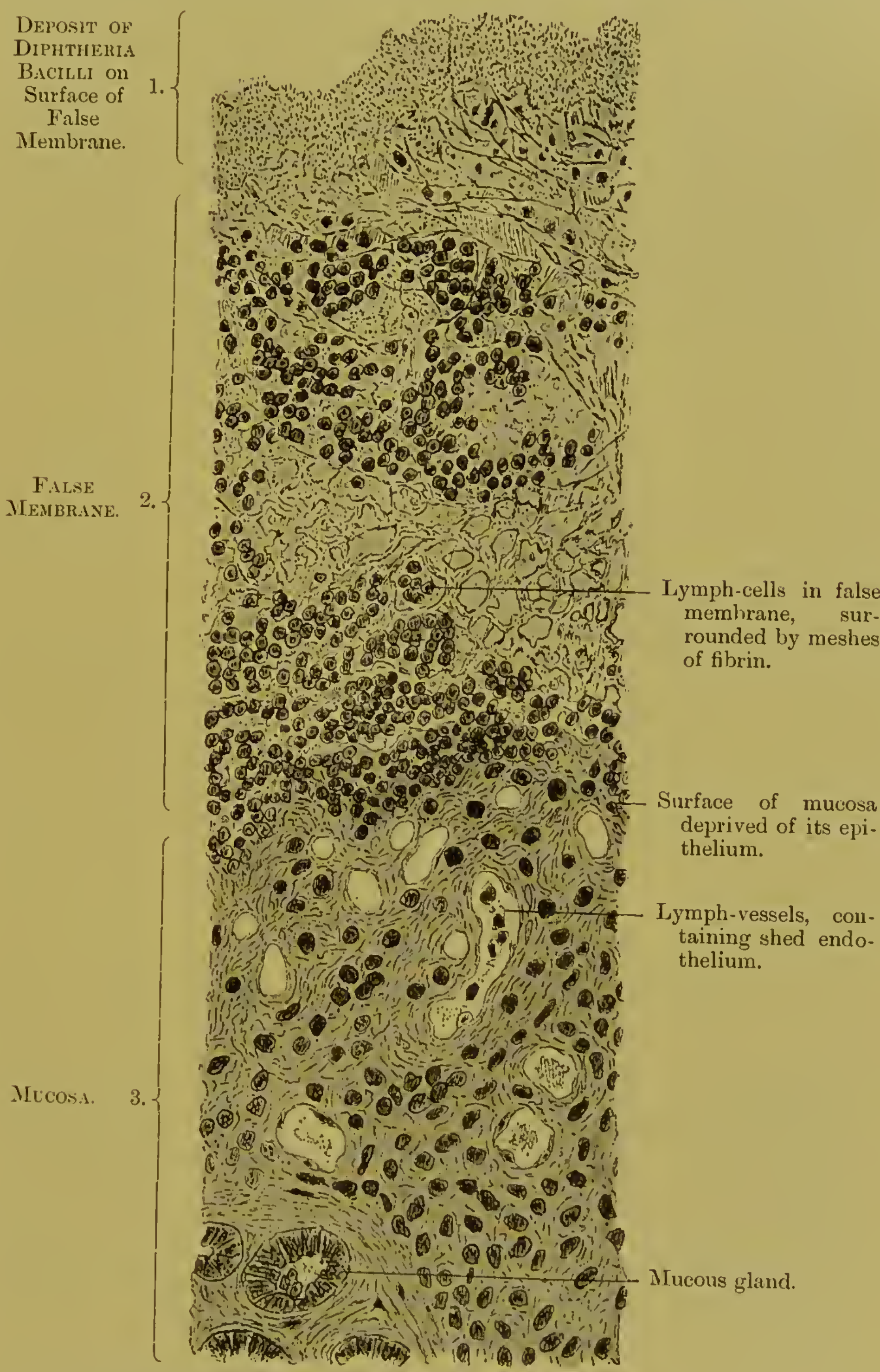

Fig. 19.—Free Surface of Diphtheric Larynx (× 350 Diams.) (*After* Hamilton.) By kind permission of Messrs. Macmillan & Co.

albumen, coagulates into a tough, firm, and elastic layer. This superficial layer is filled with buccal microbes — mostly indifferent — along with distinct little heaps of characteristic bacilli, some of which are also found imprisoned in the fibrin at a somewhat deeper level.

The bacillus of diphtheria is, in fact, found most abundantly in the superficial layers of the membrane; it may also be present in the deeper parts, but is rarely found beyond the immediate vicinity of the site (Fig. 20).

On the surface, as well as in the stratum between the false

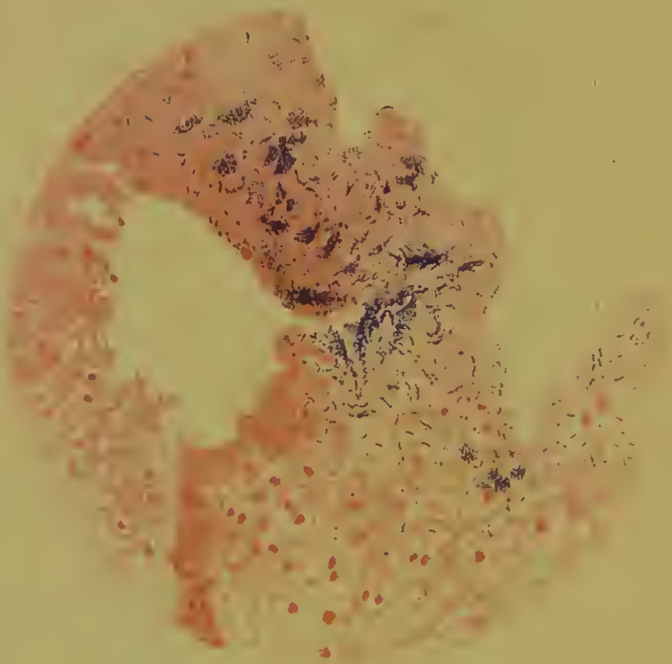

Fig. 20.—Diphtherial Membrane (Pure). Bacilli *in situ*.

membrane and the denuded epithelium, the streptococcus pyogenes and staphylococcus aureus and albus are also very frequent companions of the bacillus (Fig. 21); these organisms, unlike the bacilli, travel much further into the deeper tissues, as well as to the lymphatics and blood vessels, when they constitute the cause of secondary infective processes in the lymphatic glands, lungs, spleen, &c.

The lower strata of the mucous membrane are also invaded by the exudation, and the coagulation process extends

deeply into the sub-mucous layers, which become infiltrated with small inflammatory cells, leucocytes, and micrococci. By this process the membrane becomes progressively firmer and tougher by each fresh deposit from beneath. Thus, the external or upper layer of the diphtherial false membrane which is oldest, when it becomes disintegrated, is thrown off in the form of a slough. The subjacent epithelium soon disappears, and on the denuded surface a layer consisting of small cells, pus cells, and granular *débris* is formed, separating it from the dead material above.

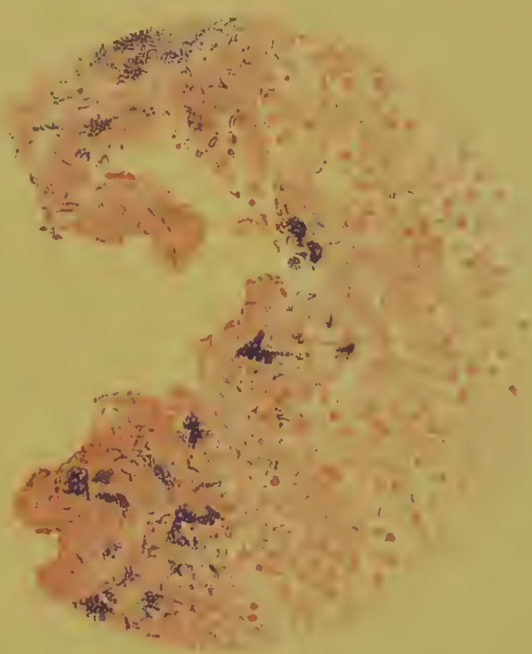

FIG. 21.—DIPHTHERIAL MEMBRANE (COMPLEX). BACILLI AND COCCI *in situ*.

The destructive process, extending deeper to the sub-mucous tissues, involves the blood vessels and the lymphatic channels.

The blood vessels become constricted from pressure, local thrombosis and embolism follow, with ulceration, necrosis, gangrene, and extravasation of blood. The lymphatics of the part are filled with leucocytes, pus cells, and cocci, which, passing into the nearest lymphatic glands, produce swelling from infiltration of inflammatory cells, and finally suppuration.

The diphtherial exudate is adherent, and can only be removed

by the employment of some force, when a raw, inflamed, and bleeding surface is exposed.

The membrane varies much in its colour, from that of white, faintly tinted with a pearly grey or lemon, to deep greyish green, brown, or almost black, the intensity of hue depending partly on the age of the exudate, and largely on the amount of blood extravasated.

The diagnostic characteristic of a true diphtherial exudate is, that it contains the Klebs-Loeffler bacillus, the presence of this organism being an irrefragable indication of the nature of the disease. When the malady marches towards cure, the bacilli diminish in number, and very often disappear with the membrane. On the other hand, they may persist long after the individual is apparently cured.

Pseudo-diphtherial membrane is characterised by an excessive production of fibrinous material, which forms a network of delicate strands and fibres, enclosing in its meshes leucocytes, granular *débris*, and pus cells. The false membrane is attached by thin fibrinous threads to the surface of the tissues beneath. The exudate is largely soluble in dilute acetic acid.

The epithelial cells become altered in character, swollen, and undergo fatty degeneration; they desquamate freely.

The membrane being only loosely adherent, can be easily stripped off, revealing a hyperæmic, but not a bleeding base. The necrotic process does not involve the entire epithelial surface, for on removal of the exudate, some patches will be found to be normal in character and unaffected.

As extravasations of blood into the interstices of the membrane are exceptional, pseudo-diphtherial exudation rarely presents a brown or black colour, but is usually of a whitish yellow, or greyish appearance.

Lastly, although streptococci, staphylococci, and other micro-organisms may be, and often are present, the bacillus diphtheriæ is conspicuously absent, this last circumstance being the criterion of differentiation.

CHAPTER VI.

BACTERIOLOGICAL DIAGNOSIS OF DIPHTHERIA AND ITS ASSOCIATES.

WITH the advance of bacteriology as a science, it has been repeatedly stated that it is impossible to make any exact diagnosis as to the diphtherial or non-diphtherial character of a membranous sore throat by clinical evidence alone.

Although in our belief that dictum has emanated for the most part from bacteriologists of but limited clinical experience, we have already recognised that the facts ascertained by a bacteriological examination are capable of exercising a marked control on a bed-side diagnosis in the way of confirmation or correction. On this account we give this aspect of the question the precedence.

The bacteriological diagnosis of diphtheria may be classified as follows :—

(1) **By a rough and ready method**, the presence or absence of the diphtheria bacillus may be decided within a few minutes of first seeing the patient, or at least immediately on the return of the physician to his consulting room. Roux and Yersin consider this method conclusive whenever the results are positive.

(2) **A provisionally negative diagnosis** may be made by the absence of the characteristic colonies of the bacillus in a culture tube, after an incubation of 24 hours at a temperature of 37° C.

(3) **A provisionally positive diagnosis** may be given by the naked eye appearances of a colony of the diphtheria bacillus similarly obtained.

(4) **A provisional diagnosis, positive or negative,** of those micro-organisms, which are the more or less frequent **associates**

of diphtheria, may be determined by the presence or absence of their colonies, after incubation of a culture on blood serum for more than 24 hours.

(5) These provisional diagnoses can be rendered **certain** by **the microscope.**

(6) By the **process of sub-culture** the bacilli may be obtained **pure**, and **the degree of their virulence** may be estimated by experimental injections into lower animals.

It is of first importance, in making an examination of throat secretions or exudations, that, whatever the method pursued, no local antiseptics should have been employed for some hours previously. Neglect of this precaution may render the diagnosis entirely futile.

Method 1.

A portion of the membrane or suspicious exudate—preferably from the site where the membrane is oldest—is removed by means of a piece of absorbent cotton wool, twisted round the end of a piece of thick wire, or held by a pair of forceps. The cotton wool swab is then wrapped in oilsilk—previously passed through boiling water—or placed in a sterilised test-tube, and in this is either carried home, or sent to a laboratory.

The next step is to pick up by dissecting forceps a small portion of the membrane thus obtained, and to dry it by means of blotting-paper. Still held by the forceps it is then rubbed over the surface of a clean cover-glass.

The film is then allowed to dry, and the cover-glass is passed lightly through the flame of a spirit lamp three or four times to fix the film to the glass.

The film is next stained with Loeffler's blue, gentian violet, or by Roux's mixture of dahlia violet and methyl-green. [For details of preparation see Formulæ, Chapter XIII.]

By using this combined stain of Roux, the specific bacilli of diphtheria are coloured much more rapidly and intensely than the other accompanying buccal microbes.

The method of staining the film is as follows:—Two or three drops of the staining fluid are dropped on the prepared cover-glass, and allowed to remain in contact with the displayed exudate for a few minutes. The excess of the stain is then washed away with a gentle stream of water, the glass lightly dried with blotting-paper, and mounted for examination under the microscope. An immersion lens should be used.

The bacilli of diphtheria, if present, should be at once recognised by the typical characters which have already been so minutely described and illustrated; but the following may be here recalled as among the most noteworthy and constant characteristics:—The gathering together of the bacilli into small clumps or groups, often of three and four, lying parallel to one another, but seldom end to end. The arrangement by which two of the bacilli form an obtuse angle, and recall the form of an open letter, V, or of a circumflex accent; while other groups resemble the letters, N, M, W, Y, and X; also T and L. These points of identification are almost more useful for this quick method of diagnosis, than the actual shape or size of the rods themselves; though these as well as the clubbed ends and the segmental staining, will further help to a diagnosis of greater accuracy.

In the majority of cases, the bacilli are so numerous that the nature of the case is at once evident; but in others, where they are more scattered, the manner in which they group themselves is so distinctive, as to almost ensure against a mistake, even by a tyro.

Louis Martin has well likened this grouping of the bacilli, to the manner in which a number of small pins arrange themselves if allowed to drop in little heaps on a table.

By this simple method not only may the bacilli be detected but, to some extent, their association with other organisms of prognostic importance may be determined.

All these must be noted. Are they streptococci, staphylococci, or diplococci, including the variety called the Brisou coccus, or are they ordinary mouth microbes, some of these which much resemble

the diphtheria bacillus, and are mainly to be distinguished by the much deeper stain taken on by the latter, and by the differences of group arrangement? If no diphtheria bacilli are found, then it should be noted what other microbes are present. If streptococci, what is their arrangement, *Rigid*, *Flexuous*, or *Batallion?* These cocci may give trouble when they are numerous, and the diphtheria bacilli are few; but at least they indicate that antiseptic precautions should be observed with more than usual vigilance.

An objection that has been raised against the cover-glass method is, that since the mouth microbes are to some extent revealed, the average eye is apt to be confused by the multiplicity of organisms. However, this can be avoided by using Gram's selective method of staining, which, only revealing the bacilli, cocci, and pneumo-cocci, does not affect the buccal microbes, which are therefore invisible. Here, then, is another valuable point in diagnosis.

Another objection to this rapid process is, that while in many cases the presence of the bacillus is satisfactorily demonstrated, a negative result may be obtained, due to the fact that there happened to be no bacilli on the cover-glass preparation, and especially may this occur when there is little or no membrane, and the swab only brings away secretion and mucus. Where this doubt exists, a diagnosis cannot be conclusive until one of the more exact methods has been adopted.

But should the typical diphtheria bacillus have been recognised by the aid of the microscope, we need go no further. The whole process has not occupied many minutes.

Method 2.

Presuming that bacilli have not been found on microscopic examination, or that we are desirous of a more complete diagnosis, we proceed to make a streak culture.

The best medium hitherto employed is the solidified blood serum, which can be obtained sterilised in tubes, ready for use,

from the Clinical Research Association, from the Institute of Preventive Medicine, or from any bacteriological laboratory.

Although the methods of carrying out these procedures will be briefly outlined here, those who have not had the opportunity of making themselves acquainted with this science, or who have not leisure to pursue it, will probably prefer to have the examination made by an expert, it being always remembered that the actual sowing of the seed must be done by themselves at the bedside.

The culture may be of two kinds, either by the **swab** or by the **needle.**

The apparatus for employment of the **swab** culture is supplied on application from any of the sourccs already enumerated.

It consists of two sterilised glass tubes, one containing the swab, the other the culture medium.

The swab is taken out of the glass tube in which it is sent, and the patient's tongue being depressed, the cotton brush is rubbed freely over the mucous membrane of the pharynx and tonsils, and especially against any visible membrane, that oldest being preferably selected; without laying the swab down, the rubber cap and wool plug are removed from the culture tube and retained between the fingers, so as to prevent contamination. The swab should then be inserted, and that portion of it which has touched the membrane, or the pharyngeal or tonsillar surfaces, should be lightly but thoroughly rubbed all over the surface of the culture medium, taking care not to break it. The swab should then be replaced in its own tube, and both the tubes should be carefully replugged and covered.

The **needle** or **streak** culture is made by picking up a minute portion of the false membrane or exudation by a special spatula-pointed platinum needle, and having removed the cap or cotton wool plug from the culture tube, two or three lines are drawn, parallel and close together, with just sufficient firmness to mark but not to disturb the surface of the serum; then, without recharging the needle, similar cultures should be made on one or two other culture tubes.

In from fourteen to eighteen hours—if the ease be one of true diphtheria—the eolonies of the baeillus first beeome apparent and characteristic; and, in the opinion of Roux, if there be no such appearance within twenty-four hours, a negative diagnosis may be formed,—at least as to that particular eulture. But here again we are not justified in saying that the membrane under examination has not been formed by the diphtheria baeillus, until repeated cultures have been made from it.

Method 3.

Presuming that our colonies have developed, how are we to know that they are those of the diphtheria bacillus ?

After the eulture tubes have been in the incubator at a temperature of 35° to 37° C. for fourteen to eighteen hours, eolonies of the **diphtheria bacillus** appear, as whitish-grey speeks, eaeh about the size of a pin's head; the contour is regular and the surfaee dry. By transmitted light the eentre of the eolony is seen to be thicker and more opaque than the periphery, which is translueent.

An almost positive diagnosis of the presence of the diphtheria baeillus is therefore established, that is to say, a **positive naked-eye** diagnosis has been obtained.

Method 4.

After twenty-four hours other mierobes form colonies, and may eomplieate the diagnosis; for example, the colonies formed by the **Brisou coccus** bear a eertain resemblance to those of the baeillus diphtheriæ; but they are smaller, the surfaee is moist, and their periphery is more opaque than the centre. The mieroscope, of course, is the *sine qua non* of accurate distinction between them, and should always be employed to control the diagnosis. The Brisou coeci appear as diplococci and cocci in rosettes, threes, fours, &c. (Fig. 10).

The **streptococcus** is of much slower growth, and its colonies

may be distinguished from those of the bacillus by the fact that they do not begin to form until the lapse of at least twenty-four hours. They appear as white colonies, very much smaller than those of the bacillus, resembling, as compared to the pin heads of colonies of the latter, so many pin points.

The staphylococcus resembles the streptococcus in its slow rate of growth; its colonies are much larger than those of the bacillus diphtheriæ. They are of a flocculent or snow-white appearance, darker in the centre, but thinner at the edges, and the halo-like effect at their periphery is somewhat increased over what is observed in a colony of the Klebs-Loeffler organism. These colonies often take from two to three days to develop properly. A yellowish or golden tint may appear in some cases, but it is by no means either an early or a constant occurrence.

A preference has been expressed for blood serum as a culture medium, because on it the diphtheria bacilli seem to grow more rapidly, and to preserve more of their special characteristics than they do when developed on agar-agar, glycerine-agar, gelatine, &c. Dr. Hayward has advocated solidified hydrocele fluid, long known as a culture medium, as of especial value for cultivation of the diphtheria bacillus, and Dr. Powell White has greatly simplified and accelerated the process by which this medium can be prepared. The advantages which these two workers claim for the hydrocele medium are:—

(1) It is easy to obtain and prepare.

(2) It is perfectly transparent, and forms a firm, clear, and solid nutrient medium.

(3) It is especially suited for the separation of the diphtheria bacillus, which grows readily upon it, and in the same forms as on the blood serum. Dr. White has "obtained a distinct growth after only seven hours' incubation."

(4) It is inimical to the growth of many of the associated organisms of diphtheria.

Streptococci grow on hydrocele fluid much more slowly than the diphtheria bacillus, not being observed for three or four days, while staphylococcus aureus grows so very slowly, and with less disposition to produce the yellow coloration, as almost to put it out of court.

It follows, therefore, from the foregoing observations, that it may be of advantage, when making cultures from suspected cases of diphtheria, to control the culture made on blood serum by another culture made at the same time on hydrocele fluid.

METHOD 5.

In making a microscopic examination of a colony, it is well that it should be done at an early stage, before the medium has been invaded by the growth of associated organisms; in other words, almost so soon as any growth is evident on the culture-medium. Details of the procedure are superfluous, and the various microscopic appearances have already been detailed.

METHOD 6.

Sub-cultures are made from the original cultivation, in a manner precisely to that already described in Method 2.

These are especially valuable when it is desirable to eliminate the bacillus from colonies of other micro-organisms with which it may be associated, and also when the microscopical appearances of the first culture suggest that the bacillus has become attenuated or non-virulent.

After making a sub-culture from such a growth, and proceeding to test the resultant diluted with bouillon by injection of a rabbit or guinea-pig, it is said that these attenuated bacilli are invariably innocuous; but we have no personal experience of this experiment.

We have now described—we trust with sufficient detail—the life history of the specific organism of diphtheria, and of the organisms of significance with which it may be associated, as well

as the methods by which a bacteriological diagnosis may be made. The following table includes twelve varieties of membranous sore throat, the nature of which can be bacteriologically determined. It comprises most of those of pure diphtheria, complex diphtheria, and such as may occasionally and reasonably be mistaken for diphtheria. The classification is based rather on the preponderance of the particular organism present, than as actually containing only those that are named in each class.

Class I. Diphtheria (simplex).
,, II. Diphtheria bacillus with streptococcus.
,, III. Diphtheria bacillus with strepto- and staphylococcus.
,, IV. Diphtheria with strepto- and diplococcus.
,, V. Diphtheria bacillus with diplococcus.
,, VI. Streptococcus.
,, VII. Strepto- and diplococcus.
,, VIII. Staphylococcus.
,, IX. Staphylo- and diplococcus.
,, X. Diplococcus.
,, XI. Diplococcus and a mycelium.
,, XII. Indeterminate.

Without anticipating the histories of our cases in detail this chapter may be fitly concluded by a brief preliminary record of those specially selected to illustrate various points of interest; and in this conjunction by comparison of the bacteriological features with the bedside diagnosis.

This table very satisfactorily demonstrates the general agreement of a bedside diagnosis with that obtained by a bacteriological examination, it being understood that in each case the latter was made independently and entirely without knowledge of any clinical details.

In one instance (No. 12), a bacteriological examination of the secretion taken from the fauces failed to detect the presence of the specific bacillus of diphtheria; nevertheless, a culture made

Class.	No. of Case.	Sex.	Age.	Clinical Diagnosis.	Bacteriological Diagnosis.	Remarks.
I.	1	F.	8	Diphtheria.	Bacillus diphtheriæ.	
„	2	M.	8	Ditto.	Ditto.	
„	3	F.	13	Ditto.	Ditto.	
„	4	M.	25	Lacunar tonsillitis of insanitary origin.	Ditto.	No paralytic sequelæ. Three-and-a-half months later non-virulent bacilli found on wound formed by removal of tonsils two days previously.
II.	5	F.	3	Malignant diphtheria, probably connected with scarlet fever.	Bacillus diphtheriæ associated with streptococci.	Intense adenitis resembling *angina Ludovici.*
„	6	M.	13 mos.	Malignant diphtheria.	Ditto.	
„	7	F.	6	Diphtheria.	Ditto.	
„	8	F.	6	Ditto.	Ditto.	
III.	9	M.	6	Diphtheria following scarlet fever.	Bacillus diphtheriæ associated with strepto- and staphylococci.	
„	10	M.	6	Diphtheria.	Ditto.	
„	11	M.	3	Ditto.	Ditto.	
„	12	F.	2	Otorrhæa following diphtheria.	Ditto.	Bacteriological report on primary throat exudate was negative of diphtheria, but acknowledged presence of staphylo-, strepto-, and other cocci.
IV.	13	F.	40	Diphtheria; possible scarlet fever taint.	Bacillus diphtheriæ associated with strepto and diplococcus.	Patient night superintendent in infectious fever hospital.
V.	14	F.	5	Diphtheria.	Bacillus diphtheriæ associated with diplococci.	Membrane not finally cleared until the twentieth day.
VI.	15	F.	29	Pseudo-diphtheria of scarlet fever.	Streptococci (flexuous variety).	High temperature during progress of the attack. Desquamation.
„	16	F.	$10\frac{1}{2}$	Ditto.	Ditto. ditto.	Ditto. Throat very characteristic of scarlet fever.
VII.	17	M.	42	Insanitary faucitis and peritonsillitis.	Streptococci (short and rigid variety) and diplococci.	
VIII.	18	M.	27	Pseudo-diphtheria of enteric fever.	Staphylococcus and bacilli *not* of diphtheria.	Death from perforation of the bowel.
„	19	F.	40	Exudative faucitis, non-diphtherial.	Staphylococci.	A curious feature was the presence of much tenacious mucus.
„	20	F.	22	Insanitary tonsillitis.	Staphylococci, with a few attenuated and stunted bacilli of diphtheria.	Two bacteriological examinations from another source failed to detect diphtheria.
IX.	21	M.	21	Œdematous faucitis and peritonsillitis, of insanitary character.	Staphylococci and diplococci.	
X.	22	F.	15	Acute lacunar tonsillitis.	Mainly diplococci.	A test case of the diphtherial character of this form of tonsillitis.
XI.	23	M.	52	Pseudo-diphtheria; marasmoid.	Cocci in pairs; non-diphtherial in chains, and fragment of a large fungus.	Chronic alcoholism, disease of heart, kidneys, and liver.
XII.	24	M.	4	Acute lacunar tonsillitis.	Varieties of cocci with non-diphtherial bacilli, and suggestions of fungus growth.	Reflex laryngeal cough without laryngeal exudation.

from an aural discharge, which occurred 14 days after admission, demonstrated the presence of the diphtheria bacillus in association with pyogenic cocci. We have knowledge of two other analogous cases, each of which were followed by typical paralysis. On the other hand, the diphtheria bacillus was found of the long variety, that is, of the kind which is beginning to be recognised as indicating a virulent form of the disease, in a case (No. 4) clinically diagnosed as non-diphtherial: no paralytic sequelæ followed, and non-virulent bacilli were found on the faucial wound two days after tonsillotomy three and a half months later.

One more illustrative example is afforded in *Case* 20: the patient was certified into hospital by an experienced practitioner as one of probable diphtheria. On clinical evidences we had no doubts as to its being pseudo-diphtherial, but the bacteriological reports were not quite unanimous. Two repeated examinations of separate cultures failed to detect bacilli. Another independent examination revealed a very few short, stunted bacilli (Fig. 51). The patient made a rapid recovery, without sequelæ.

It is true that a suggestion has been made that paralytic sequelæ may possibly occur in throats that are coccal and not bacillary, the opinion being held that paralysis is not necessarily proof positive that the case has been one of true diphtheria. In the present state of our knowledge it is impossible to substantiate such a position. In any case, the occurrence would be most exceptional, and could only be entertained after a rigid process of exclusion. It has, however, been pointed out by Sims Woodhead, Thresh, and others, that the negative evidence of diphtheria is sometimes contradicted by positive clinical symptoms exhibited by the patient during the course of the malady. These circumstances are mentioned to demonstrate that the bacteriological diagnosis is not always so infallible as has been advanced in some quarters, but we would not for a moment claim that these exceptional discrepancies are of sufficient frequency to cast any general discredit on the direct testimony to be gained from the laboratory.

CHAPTER VII.

THE CLINICAL DIAGNOSIS OF DIPHTHERIA AND ITS ASSOCIATES.

HAVING occupied ourselves in the preceding chapter with a consideration of those points of diagnosis which can be solved by bacteriology, we now turn to those elements of diagnosis which should be familiar to, and adopted by, every well-informed practitioner on his first interview with any patient supposed to be suffering from diphtheria.

It is a common experience of everyone connected with hospitals where diphtheria is treated as an infectious disease, and with those consulted in such cases, for their aid and opinion to be sought by persons who are supposed to be the victims of diphtheria, but who, on quite cursory inspection, are recognised as suffering from some more simple malady. Such mistakes require to be very charitably considered, for obvious as they now and then may appear to the expert who sees the case for the first time late in its history, there is probably no throat affection more protean in its clinical disguises, and more deceptive in its initial stages than is diphtheria.

Of a quite separate category are those inflammations of the throat accompanied by exudation of pseudo-membrane, which occur during the course of the specific fevers. Until the elucidation afforded by bacteriology, these have been considered by the majority of authors from the time of Home in 1765, to be truly diphtheric, notwithstanding many vigorous and weighty arguments to the contrary. We now know, as has been mentioned more than once already, and as we may have occasion to repeat

more than once again, that the membranous inflammations of the throat exhibited previously to, or during the early stages of any of the exanthemata, are not, as a rule, of the nature of true diphtheria; while such as are implanted on them in defervescence or as sequelæ, are almost invariably proved to be absolutely of that nature by the presence of the Klebs-Loeffler bacillus.

As a direct result of bacteriological enthusiasm there is a general confession, on the part of recent authors, that the clinical evidences of these diseases, at least so far as they are afforded in the throat, are so difficult or even impossible of distinction, as only to be settled by a culture and a microscopical examination.

To such a wholesale surrender of our clinical fortress we cannot for a moment submit; though it must be frankly conceded that, not rarely, cases occur in which the most experienced clinical observer may find himself at fault.

To render these occasions less frequent an attempt will be made to demonstrate that these doubts can be solved, in a large degree, by a careful comparison of the symptoms, both physical and functional, of those membranous sore throats which are characterised by the micro-organism recognised as specific of diphtheria, either alone or in association with cocci; and by due recognition of other more special evidences of the different diseases in which they are found.

If the clinician would work with the bacteriologist on these lines it ought not to be long before the occasions on which an error in diagnosis on the part of the former has to be corrected by the researches of the latter, will become so rare as to be exceptional. On the other hand, it is with deference suggested that it would be well if the bacteriologist would make it a more general practice to visit the wards, and be thus enabled to compare the conclusions formed in the laboratory with the data afforded at the bedside of the patient.

The following are the special points on which information should be obtained before proceeding to an examination of any case suspected to be diphtheria:—

The age of the patient.

The number of members in the family.

The pre-existence of similar throat affections among its members.

Evidence of exposure to infection by personal communication, or otherwise.

History of recent attacks of diphtheria in the household, or of any of the diseases in which sore throat is a symptom, or which are recognised as predisponents to diphtheria.

Finally, the condition of the sanitary surroundings of the patient.

Next, inquiry should be carefully made as to the exact date of the initial symptoms, in order to determine the probable period of **incubation.** The experimental incubation period, when communicated by inoculation in the lower animals, is short, and varies from twelve hours to three days. It is said to be about the same period when a human patient is infected by direct contact, and our own experience leads us to concur that the disease is not infrequently developed at the minimum interval.

Leslie Phillips reports a very interesting case in which some of the same instruments were used on the same day, first in the operation for tracheotomy for diphtheria, and secondly for circumcision; the circumcised child had pseudo-membrane on the prepuce on the fourth day.

In ordinary circumstances, the period between the exposure to the contagion and the appearance of false membrane in the throat is probably from one to four days. A longer interval is exceptional.

Evidence as to the mode of onset, whether sudden or gradual, is of great importance; the former being the rule in diphtheria, especially among infants and very young children. In those over 10 years of age and in adults the development may be slower.

Having satisfied ourselves on these points, we shall now, by a brief description of the symptoms, proceed to indicate the diagnostic value of each.

The **prodromata** are: *general malaise*, quickly followed by *headache, nausea, pain in the back* and *limbs, concurrently* with the early throat symptoms. The invasion is *rarely* marked by *rigors* in children, as mentioned by Schech, for such a circumstance is as unusual in this as in any other disease of childhood.

Vomiting is only an occasional, and by no means so constant, a forerunner of diphtheria as of scarlet fever. *Diarrhœa* is, sometimes, present, but the opposite also obtains. The *neck* is sometimes complained of as feeling stiff, with *pain* at the angle of the jaw, but neither within the throat itself, on opening the mouth, nor in swallowing, is there either appreciable pain or difficulty experienced, thus differentiating the malady from ordinary forms of tonsillitis; and, indeed, this absence of pain is of valuable diagnostic significance. Within a few hours of these first symptoms, or—exceptionally—after a longer time, the special local manifestations in the pharynx become obvious; the throat feels dry, and there is a desire to hawk and clear the fauces. The *voice* is often distinctly hoarse and rough, even before there is membrane in the larynx, and should this have spread to that situation before the patient is seen, vocal tone may have been altogether lost. With this, there will be observed also a *laryngeal cough*, noisy *stridor*, and *dyspnœa*, due to obstruction, with exacerbations of true spasm.

The *tonsils* and *fauces* are, as a rule, first attacked, being generally red, swollen, and thickened; they soon become the seat of patches of exudation, which can be observed to increase in thickness, to become tougher in consistence, and to extend, sometimes rapidly, in area. Detailed description of the exudation is for sake of convenience deferred. There is very little which is distinctive in the appearance of the *tongue*, but one should note the absence of the thickly furred and foul surface, seen in ordinary tonsillitis; and bear in mind the equally distinctive appearances of this organ in scarlet fever.

Young children, who are the subjects of diphtheria, present at a very early period in the attack a particularly characteristic *pallor*

and *waxiness* of the complexion, with a pinching of the nostrils. Sometimes they are fretful, but even in the early stages are far more often *listless* and lethargic, and they seldom give any indication, either by their temper or actions, of acute pain; all these symptoms being indicative of the *asthenic* character of the disease.

An *erythematous* eruption on the trunk, and "blanket" rash is, although not common, sometimes to be noted in diphtheria; albeit, it is particularly evanescent, such a rash may obscure or confuse an exact diagnosis.

The *nostrils* being not infrequently implicated, their normal functions are interfered with, and fluids may escape through the nose during swallowing, even before the palatal muscles have become paretic. *Nasal discharge,* when present, is usually of a peculiarly fœtid, sanious, and irritating character; and is of diagnostic import. It is, therefore, important to examine the nares for membrane, for which purpose, if the lumen be obstructed by mucus, a warm alkaline douche may be first employed. *Epistaxis,* always a grave symptom, is by no means uncommon.

When the posterior surface of the *uvula* is the site of exudation, the posterior nasal space is almost always involved. Exudation rarely commences in the anterior nares.

The temperature in cases of diphtheria is usually low in comparison with the acuteness of the constitutional disturbances characteristic of the disease. From our table of 1000 cases which came under observation, on an average, on the third day of the diphtherial attack, the temperature in 80 per cent. was 101° F., while in 50 per cent. the average temperature during its course was below 99° F.

Acute adenitis, as a complication in the course of an attack of diphtheria, is attended by a rise of temperature, sometimes to the extent of 104° to 106°, but the hyperpyrexia quickly subsides, except in those cases where suppuration ensues, and then on liberation of the pus. When diphtheria is complicated with any of the exanthemata, the temperature chart

frequently partakes of the particular characteristics of the associated disease.

But independently of these circumstances, the thermometer gives indications of the first importance in diphtheria, and, indeed, there are few diseases in which it affords greater aid, albeit the variations are but rarely extreme. As a rule, an increase may be taken to point to a further extension of membrane or a complication; reduction within certain limits is a sign of improvement.

Commencing with a more or less rapid rise, rarely exceeding 102° F., the temperature is immediately lowered on the appearance of false membrane, and falls to normal, or a point or two below it—a fact which is readily accounted for by the asthenic character of the malady. A further rise may give warning of an *Adenitis*, which we have already considered, of *Nephritis*, *Otitis*, or of *Broncho-pneumonia*; it may also indicate the occurrence of *Paralysis*, or may be premonitory of *Cardiac* implication, when we may soon witness a sudden and serious fall below the normal. This subsidence is to be taken as an almost unfailing premonition of death by *Asthenia.*

The distinguishing feature in the **pulse** of diphtheria is its extreme rapidity in proportion to the temperature; this is much more marked than in scarlatina, in which the temperature is distinctly high, and for a longer period. Both the rate, force, and regularity are influenced by the profound asthenia which characterises the constitutional toxæmia, and an abnormally slow pulse indicates complications, the gravity of which will be considered under the elements of prognosis.

Adenitis.—The character and situation of inflammatory enlargements of the lymphatic glands next claim our attention as being of almost constant occurrence in pharyngeal diphtheria, and of considerable diagnostic importance.

There is a distinct difference in the portion of the glandular region affected.

In true **simple diphtheria**, the **cervical** glands are those mostly attacked. This may be in the form of enlargement and

tenderness of the whole chain of glands, which can be separately felt; or, in the gravest cases, as one large swollen mass in the neck, in which the **parotid** may also be involved.

In **complex diphtheria, both** the **cervical** and **sub-maxillary** glands are affected; and in **pseudo-diphtheria**—that of scarlet fever, for example—the sub-maxillary glands are those most frequently affected. In diphtheria, following scarlet or other specific fever, or in any circumstances in which streptococci are associated with the diphtheria bacillus, both sets of glands are liable to be inflamed concurrently (*Case* 5).

Adenitis is far more common in scarlet fever than in diphtheria; indeed, it may be taken as one of the ordinary symptoms of the former disease. It is far more intense, and suppuration, to which it is also more prone, takes place at a much earlier date. Nevertheless, suppurating adenitis and cellulitis are far more frequent in true diphtheria, especially in the cocco-bacillary varieties, than is generally thought; for this complication, or—as it may almost be termed—this sequela, was found in 9·75 per cent. of our 1000 cases.

Albuminuria.—The quantity of urine excreted, and its specific gravity, are to be noted night and morning, with efficient tests according to indications. The presence of albumen in the urine is not of great diagnostic importance in diphtheria. True, it is present in about one-third of all cases, but it is likewise to be found in many other varieties of inflammation of the throat of non-diphtherial nature. The prognostic significance of albuminuria may be deferred. The urine in diphtheria contains an *excess of urea*, and, in the majority of cases, epithelial cells and casts; but *hœmaturia* is rare by comparison with its frequency in scarlet fever.

Renal complications are an early manifestation in diphtheria, as compared with those of scarlet fever. There are, however, exceptions to this sequence in both directions.

Some perversion of function of the special senses of *smell, taste*, and *hearing* will often be found if carefully looked for.

The *odour* of the *breath* is not always tainted, but in malignant

cases is so extremely offensive that no caution is necessary in regard to the danger of inhaling it.

It is important that the practitioner should satisfy himself on all the foregoing data before he proceeds to examine the throat minutely. This is our next step.

We have already noted that the fauces are more or less inflamed in patients attacked with diphtheria, though the hyperæmia in the case of this disease is always of a lower grade than in that of a throat manifestation in connection with scarlet fever or measles. It is quite exceptional for diphtheria to exist without more or less exudation in some portion of the air passages; and we shall therefore, in further investigation of this region, assume that membrane is present in the cases under our observation for the purpose of diagnosis.

And first as to **the site of the membrane**. Valuable information on this point may be gained by an analysis of 1000 consecutive cases of diphtheria, to which we have already taken occasion to allude for statistical purposes on other points of clinical interest.

TABLE *of* 1000 *cases of diphtheria, showing the relative frequency of sites of the membrane.*

PART AFFECTED.	NO.
Fauces (alone),	672
Larynx ,,	4
Nostrils ,,	2
Fauces and Larynx,	109
Fauces and Nostrils,	165
Fauces, Larynx, and Nostrils,	46
Labial or Buccal only,	1
Hard Palate only,	1
	1000

NOTE.—There were six cases in the series in which the membrane extended into the buccal cavity and forward to the *hard* palate.

The above table speaks for itself, but there are a few points that merit expansion.

As to the **tonsils**, these were the sites in all the cases where the situation is described as that of the fauces, and this disposition to attack the tonsillar tissue is evidenced not only in the **faucial** region, but in the pharyngeal vault, where is situated the **pharyngeal tonsil**, at the orifice of the Eustachian tubes (**tubal tonsil**), at the base of the tongue (**lingual tonsil**), and, finally, in the ventricles of the larynx, the glandular tissue of which may be held to represent the **laryngeal tonsil**.

It is a peculiarity of the diphtheric exudation to start on some little prominence, such as the uvula, the free edge of the epiglottis, on the eminences of the cartilages of Wrisberg and Santorini, or in some small recess, such as those of the lacunæ of the tonsils, and of the ventricles.

As to the **larynx**, the figures in the table may be taken as rather underestimating the frequency of laryngeal extension, for in this series the laryngoscope was not employed. But admitting that a laryngoscopic examination is attended by considerable difficulties in all young children, and especially in the subjects of diphtheria, in at least 90 per cent. of whom enlargement of the tonsils proves an obstacle to a complete view of the larynx, those in which the epiglottis could not be seen must constitute a very small minority. And it is to be regretted that, at so mature a period of the art of laryngoscopy, the mirror is still so rarely employed in the diagnosis of diphtheria except by specialists. For not only would diagnosis be thereby rendered more complete, but in the matter of treatment, intra-laryngeal applications, and especially intubation—as we insisted on its first re-introduction—would be more easy of accomplishment, and attended by more satisfactory results, if the hand of the operator were habitually guided by the reflection of the larynx in the mirror.

The membrane in pure and in complex diphtheria.—The diphtherial membrane in a typical case,—although described by so careful an observer as the late Sir Morell Mackenzie, as commencing with an infiltration at certain points, of a yellow substance—in our

own experience, begins almost invariably as a thin bluish-white deposit, something like a shaving from the boiled white of an egg of the duck, goose, or plover. As the deposit increases in thickness, it gradually becomes more white and opaque, resembling the boiled albumen of a fowl's egg, or it may then partake of a very pale lemon tint. Then it becomes of a yellowish or greenish grey, brown, and sometimes almost black, as the necrotic process advances, or as blood is extravasated. Only in the comparatively uncommon case of a lacunar diphtheria do we see the exudation commencing as discrete spots of deposit, which may be of yellow colour at the very first onset (*Case* 4), and, even when coalesced, may never exhibit the pearly or opalescent appearance which characterises the more ordinary form on its first manifestation.

The membrane is sometimes "plastered," as if put on with a palette knife, or "laid on with a trowel." This is especially well seen in the illustration to *Case* 14, page 123. More commonly the deposit is of unequal thickness, occasionally leaving exposed areas of uncovered and inflamed mucous membrane (*Cases* 1 and 7).

The edges are often thicker than the centre (*Cases* 7 and 14), and when about to separate, become crinkled and everted (*Cases* 7 and 8). Shreds or strips of the membrane can be more or less easily removed by forceps, with the result of an exposure of a raw bleeding surface (*Case* 2), or of bleeding points (*Case* 3), followed, if left untreated remedially, or even in spite of treatment, by a re-formation of the membranous deposit.

A diagnostic feature of the exudation of true diphtheria is that the membrane is deposited not only on the tonsils, as in pseudo-diphtheric inflammations, but also on the pillars of the fauces, the uvula, and on the posterior surface of the uvula (*Cases* 2, 7, 8, and 10), this last situation being almost pathognomonic. This investment of the uvula with membrane is so complete that Trousseau's description of a cast of it when shed, as resembling the finger of a glove, will occur to every one as most apt. When the membrane is observed at the side or edge of the uvula, it is an almost certain indication that the whole posterior surface is in-

volved, and this can be proved by turning up the uvula with the end of a spatula.

It may also spread to the soft palate (*Case* 2), and even to the hard palate; we have, indeed, seen it lining almost the entire buccal cavity. Sometimes it invades the gums. The membrane extends backwards to the posterior wall of the pharynx, and into the post-nasal space; it may envelop the turbinals; rarely, it may commence in the anterior nares, and quite occasionally is limited to the nasal fossæ (Frontispiece). From the pharyngeal vault the membrane may extend along the Eustachian tubes (*Case* 12).

Diphtherial exudation has a far greater tendency to travel downwards into the larynx than is recognised by those unaccustomed to use the laryngeal mirror, though quite often it does not reach further than the epiglottis (*Case* 11). In these circumstances, there may be little or no laryngeal distress, but, of course, in many other cases it seriously involves the glottis, and may extend the whole way down the trachea (Frontispiece), and even to several divisions of the bronchi. Œdema, by which is meant sub-mucous effusion giving translucency to tissues of the fauces or larynx is, according to our experience, almost unknown in pure diphtheria, in this respect strongly differentiating the disease from the false varieties, especially those characterised by the presence of the milder forms of cocci. Casts, more or less complete, are constantly shed from the tonsils, uvula, and from the air-passages, and, what is not so commonly known, from the nasal fossæ (*Case* 8). When the nose is affected, the nasal discharge is either serous or sero-sanguineous; epistaxis is common, and the peculiar fœtor of true diphtheria is, by accumulation of secretion in the nasal passages, more than usually emphasised (*Cases* 2 and 6).

False membrane in true diphtheria is not all deposited at the same time, and patches of variations of exudation of different ages, and consequently of different consistence and colour, may often be witnessed at different sites in the same throat. This is well exemplified in the illustration to *Case* 1, and the circumstance is of assistance to a differential diagnosis.

It is difficult to say what, if any, are the definite clinical distinctions to be drawn between the physical appearances of the membrane of pure diphtheria and that of the impure or complex forms; but there is a decided increase of phlegmon and swelling of the mucosa in those cases in which the streptococcus is specially predominant. Particularly is this so if the organism chains itself in that arrangement indicating its most virulent form—namely, the Conglomerate or Batallion.

When these cocci so predominate, the membrane may not be by any means so abundant as in pure diphtheria, the streptococci seeming in some degree to swamp the bacillus. This feature was very marked in *Cases* 5 and 6.

The membrane in pseudo-diphtheria.—We have already remarked that a membranous sore throat, characterised by the presence of the Klebs-Loeffler bacillus, in association with streptococci, not infrequently represents a diphtheria supervening on one or other of the exanthemata, of which scarlet fever is the most common. In like manner, a sore throat, in which the streptococcus is the sole organism present, usually represents a pseudo-diphtheria of the same class of infectious fever; not, we repeat, that it is intended to affirm that the streptococcus is the specific microbe of scarlet fever, for that still remains to be discovered. In these cases, the chaining of the cocci is generally of the flexuous variety.

Streptococci in short, rigid chains, when associated with either staphylococci or diplococci, are usually characteristic of sore throats of a septic or insanitary origin, and in many of these cases there is little or no membrane present. This last point is also to be observed in some instances in which staphylococci are the predominant organisms, but as a rule there is an abundance of exudation of a much more yellow colour, than that in either the pure or complex diphtheria, or in that of the streptococcal membrane; the exudate in these circumstances, moreover, is sometimes accompanied by much viscid secretion (*Cases* 19 and 20); it does not separate readily, and when removed but a slightly hæmorrhagic

surface is exposed. In this variety of sore throat suppuration of the tonsils is of common occurrence.

Finally, with regard to the diplococcus, we have already seen that cocci arranged in pairs are not responsible for any serious form of membranous sore throat; its presence, when associated with the bacillus of diphtheria, and with other cocci of graver significance than itself, has appeared to us to retard the clearing of the throat from membrane, and to give it a somewhat "dirty" character. No more need be said on the characteristics of the exudate.

We shall now proceed to describe the chief points in the differential diagnosis between diphtheria and the pseudo-diphtheriæ which occur during the course of various specific fevers, and some of the minor forms of inflammatory sore throat, all of which may for our present purpose be considered as of pseudo-diphtherial character.

Scarlet Fever.—Inflammation of the fauces is the rule in all cases of scarlet fever, however mild their character. The throat appearances bear a strong resemblance to those of tonsillitis, and the faucial inflammation is attended by almost as much functional pain, though there is not the same characteristic locking of the jaw on attempt to open the mouth which is almost pathognomonic of quinsy. We have already alluded to the differential circumstances of invariable and early vomiting and high temperature in scarlet fever, to which we may add its more sudden onset. A distinction may be made in the characters of the skin eruption. In the rare cases of such a manifestation in diphtheria the rash is erythematous, of late occurrence, and mostly appears on the neck and chest; in scarlatina it is punctiform, an early symptom, and attacks the skin of the whole body. The circumstance of desquamation constitutes another, though naturally a tardy, element of differentiation.

It is comparatively exceptional for a scarlet fever throat to be attended with false membrane. We are not in a position to give figures in support of this assertion, but Sanné, who wrote

before the discovery of the bacillus, found membranous exudation in 95 cases of scarlet fever, out of a total number of 229, of all varieties of what he called "secondary diphtheria." The complication, whenever it occurs, is rightly interpreted as of great gravity.

The exudation is yellowish in colour, and, so to speak, dirtier, or greyer; the surrounding mucous membrane representing a more intense and extended form of hyperæmia than in true diphtheria. It cannot be stripped off in connected shreds, being rather pulpy, or, even pultaceous; it is as it were more "inlaid" (*Case* 16).

The pseudo-membrane has a tendency, as Soerensen says, to melt down into a purulent mass, and to quickly leave deep and destructive ulcers, producing characteristic perforations in the pillars of the fauces. It frequently produces suppurative inflammation of the middle ear by extension through the Eustachian tubes, this event being attended by great pain. No membrane is observed in the nose, but there is often a purulent discharge. Epistaxis is not common, but hæmorrhages from the throat are more frequent in this form than in any other, on account of the deep ravages made in the tissues. In fact, this strong disposition to bleed constitutes a marked difficulty in making a satisfactory diagnosis of the exact condition of a throat in scarlatina. Membrane extends to the air passages but rarely, and when the larynx is attacked, the inflammation is usually of the nature of an acute œdema, the results of the ulceration, for primary œdema of the throat in relation to scarlet fever is almost as rare as in diphtheria. Membranous laryngitis occurring during scarlatina is probably of cocco-bacillary origin.

Measles.—Although it may not be possible to detect very much difference in the grade of the inflammation of the fauces from that of scarlet fever, those who have had experience will readily recognise that there is almost as much distinction between the appearance of the mucous membrane of the fauces in the angina without exudation in cases of measles, and that of scarlet fever, as there is in the cutaneous eruption.

The preliminary symptom of measles—Coryza—is emphasised in those cases of pseudo-diphtheria, which occur in its course, and the disposition to pulmonary congestion and bronchitis is another distinctive feature.

Most marked, however, of all is the great redness of the conjunctivæ, and the occasional production of membrane in this situation; certainly, in a case of conjunctival diphtheria—which by the way is very rare—we should be led to look for measles as the primary disease. Faucial membrane during the course of measles is only observed quite exceptionally, though true diphtheria is more often a sequel of this exanthem than of scarlet fever, in which, as has been already noted, a pseudo-diphtheria may precede the rash. There is, also, less tendency to suppuration and ulceration of the throat; and although middle ear complications like those in scarlet fever are common—much more so than generally supposed—in measles, they usually commence as a sero-mucous inflammation, while in scarlet fever they are almost always suppurative.

Implication of the larynx and trachea is more common in measles than in scarlet fever, and occurs as a late complication. Acute membranous laryngitis (croup) without visible faucial deposits is relatively much more common in measles than in true diphtheria. In fact, as is well known, inflammation of the whole respiratory tract, and also of the alveoli, is a recognised characteristic of Rubeola.

Whooping-Cough.—Pseudo-diphtheria is sometimes found associated with pertussis, and the manifestations, both in the throat and larynx, are not dissimilar to those found in measles. Distinction will, therefore, be made by the characteristic symptoms of the parent disease.

Typhoid Fever.—A certain amount of pharyngeal and laryngeal inflammation is not uncommon in enteric fever, and if looked for, a faucial exudation, easily to be distinguished from aphtha by its microscopic features, may be seen about the third week. Independently of the special commemorative signs, the charac-

teristic point about the throat is that the membrane does not become thicker, does not separate more easily than in scarlet fever, and that it is characterised by the presence of staphylococci rather than by that of streptococci; lastly, it is altogether of a milder nature. As Morell Mackenzie has said, "though it (exudation) frequently commences in the larynx, and is often confined to that part, the diminished supply of air causes little inconvenience, owing to the medulla having, to a great extent, lost its sensibility to impressions. The obstruction to respiration is also less marked, from the fact of the disease in most cases attacking adults."

But while probably the pseudo-membrane exhibited at any stage of a typhoid attack is far less frequently truly diphtherial than it is in the case of scarlet fever or measles, diphtheria as a sequel has been occasionally recorded, and each one of these three specific fevers has often been noted as prevalent, prior to and concurrent with a diphtheria outbreak.

An interesting case is reported by Dr. Gayton to the *Lancet*, May 5th, 1894, in which true diphtherial croup supervened on enteric fever on the fourteenth day after admission for the latter. Tracheotomy was performed, and the patient, a boy of eight years, made a good recovery.

Dr. Gayton, commenting on this case, remarks that "the incidence of diphtheria during the course of enteric fever must be extremely rare, Sir William Jenner, Murchison, and others, who have written on the subject, not mentioning its occurrence."

Smallpox.—As regards smallpox, careful inquiries from those whose experience of this disease can be numbered by thousands of cases, assure me that membranous exudation of the throat is practically unknown; but it has been observed, in association with a very low and malignant type of this disease, that deep ulcerations and necrosis may occur, leading to œdema of the glottis. The same remark applies to **Typhus** fever. In fact, it is doubtful in any *post-mortem* examination made in either of

these diseases whether the larynx or trachea is ever found in a perfectly healthy state.

A mild form of membranous exudation may be seen sometimes in cases of **Chickenpox**, and although membrane is almost unknown in **Rotheln** and in **Mumps**, the congestion and hyperæmia of the mucous membrane of the fauces and pharynx in these disorders render them more susceptible to the attacks of the diphtheria bacillus. The diagnosis is not difficult in view of the general characters of the diseases.

A differential diagnosis is occasionally more difficult in cases of milder forms of throat inflammations than in the throat manifestations of the acute specific fevers, in which there are so many other marks of distinction. Thus, pharyngeal patches of diphtherial membrane may quite excusably be confounded with **aphtha** or **herpes**, with **simple membranous** inflammation, whether idiopathic or traumatic, with **exudative lacunar tonsillitis**, with **phlegmonous pharyngitis**, and with **syphilis**, especially in the very early secondary stages of this last-named specific affection, when mucous patches often bear a strong resemblance to those of diphtheria, and more particularly in those cases in which there is slight pyrexia and glandular tenderness.

We have seen in one of our cases that a pseudo-membrane may occur in low and debilitated constitutional states, and in general marasmus, which, in the instance under remark, led to a notification of diphtheria, and the removal of the patient to an infectious fever hospital (*Case* 23). The crucial test is the presence of the diphtheria bacillus, but independently of this, the history and subsequent progress of the case under observation should assist to a quick clearing up of the diagnosis.

As to **tonsillitis**, it may generally be said that it is dangerous in an inverse proportion to the severity of the symptoms; of these special mention may be made of the suddenness of onset, the high temperature, and, above all, the pain. It is worthy of repetition that the great difficulty in opening the mouth and the extreme dysphagia, so characteristic of the milder malady, will materially

contribute to a correct recognition of the nature of the case at an early stage; and long before suppuration has occurred all doubts should have been dissipated. Not so much can now-a-days be said as to the distinction between the cheesy blocking of lacunæ in tonsillitis and diphtherial membrane, for we now know that many cases, judged by this symptom in pre-bacteriological times as of the former class, are truly diphtherial. More characteristic is the fact that in tonsillitis the membrane, or rather exudate, is limited to the gland, the creamy and easily cleared secretion of which can be readily distinguished from the firmly attached fibrinous membrane of diphtheria. Finally, quinsy is accompanied by much muco-salivary secretion of a viscid and clogging character; diphtheria is a much drier disease.

With **aphtha** and **herpes**, diphtheria will rarely be confounded even by the tyro after the second visit.

As to **membranous sore throat**, apart from membranous laryngitis, we do not recognise such a disease uncomplicated by specific influences of constitution or hygiene. In **pharyngeal erysipelas**, which includes the **septic sore throat** of some authors, the temperature is higher; there is always great distress; the tissues are very œdematous and livid; the cutaneous surface of the neck is usually involved, and membrane is rarely present,—at any rate of a consistence likely to lead to a more than momentary doubt.

CHAPTER VIII.

RECORD OF ILLUSTRATIVE CASES OF DIPHTHERIA AND ITS ASSOCIATES.

The various methods known to the bacteriologist, by which the specific organism in a case of diphtheria or pseudo-diphtheria can be detected, as well as the more important elements of diagnosis at the bedside, having been now described and discussed, it appears convenient to here insert a record of cases illustrative of most of the points of interest, whether of parallelism or of apparent discrepancy from this two-fold aspect.

It is true that, to avoid repetition, the elements of prognosis and some questions of treatment are in a measure anticipated by this order of arrangement; but this, it is hoped, will be a minor inconvenience to the reader, and will be outweighed by the advantage of having a clear view of the lines on which our forecast and the indications for treatment should be laid.

CLASS I.

Bacillus Diphtheriæ.

Case 1. *Faucial exudation; serum treatment; anuria; death.*

A female child, aged 8 years, admitted to hospital on November 17th, 1894, on the third day of the disease.

Previous History.—The little patient, quite well on the morning of November 14th, and in her usual health at mid-day, returned from school in the evening complaining of headache, and of nausea even to the extent of actually vomiting. The child had lived with her parents in the same house for upwards of two and a

half years, during which time two sisters had died from bronchitis. A school companion and near neighbour, in close intimacy, had been removed to the hospital on account of diphtheria on the previous day.

On admission, the **fauces** on the **left** side were seen to be much swollen, with a **pearly white exudation** on the corresponding tonsil, which extended somewhat on to the **soft palate**. There was also thin pellicular secretion on the right side, indicating a more recent exudation at that site (Fig. 22). The **neck** was

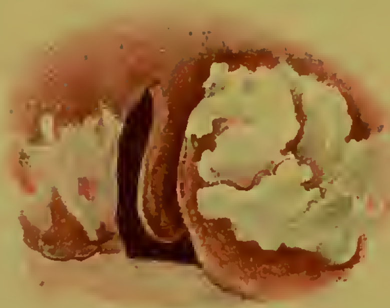

Fig. 22.

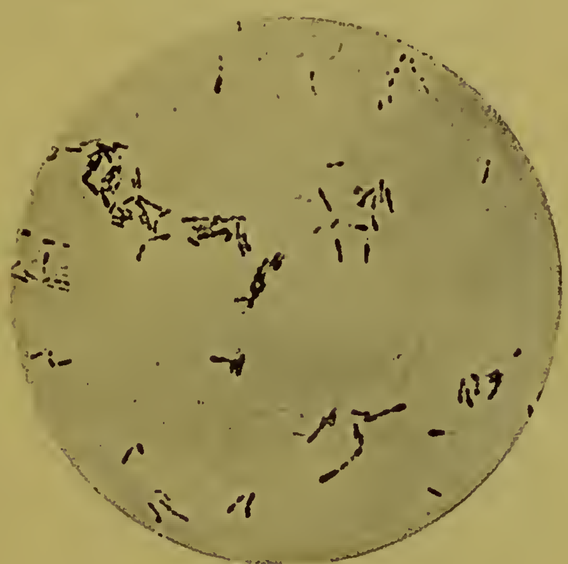

Fig. 23.

swollen more on the left than on the right side. The *temperature* was 100° F.

The **bacteriological** examination demonstrated a typical growth of the bacillus diphtheriæ, almost without any other micro-organism (Fig. 23).

On the 18th the *temperature* was 100° F. The amount of *urine* passed was 12 ounces, and contained *no albumen.* The patient slept fairly well and took her food naturally. **Rhinorrhœa** was profuse, but the nostrils were not completely blocked; nor was membrane seen in that situation. The exudation on the left side of the fauces was in process of separation. The evening temperature was 99·8° F.

November 19*th*.—A **cast** of the left tonsil was shed, leaving a thin pultaceous secretion over an apparently ulcerated surface. The *cervical* glands on both sides were swollen and tender; discharge from the nose profuse; and membrane now distinctly seen in each nostril; but fœtor was not detected. Face pallid, and waxy complexion. Temperature, 99·4°; pulse, 112; the urine contained $\frac{1}{8}$th albumen. *Deglutition* easy; very little sleep, very restless.

November 20*th*.—*Temperature*, 102·8°; pulse, 128. Vomited several times. Glandular swelling on the right side increased. Colour of face *earthy*. Eight ounces of urine, containing $\frac{1}{2}$ albumen, passed in the last five hours. The left tonsil enveloped in a thick leathery membrane. Some dyspnœa. Heart's action very feeble.

November 21*st*.—Temperature, 101·4°; pulse, 140, almost imperceptible at wrist. Membrane on fauces less; glandular swelling reduced. Erythematous rash on neck, trunk, and limbs. Only $\frac{1}{2}$-ounce of urine passed in last twelve hours. The child died at 8.30 P.M., no urine having been passed for fifteen hours.

Treatment.—**Two** injections of **Antitoxin**, from the British Institute of Preventive Medicine (**B. I. P. M.**), were administered, the first of $12\frac{1}{2}$ c.c., and the second of 10 c.c. Locally antiseptic swabbings and douching with sublimate solutions, and medicines to promote renal excretion.

At the **autopsy** the kidneys exhibited a condition similar to that observed in the first stage of acute nephritis.

Case 2.—*Faucial membrane; hæmorrhagic form; serum treatment; anuria; death.*

A male child, aged 8 years. Admitted to hospital on *December* 11*th*, 1894, on the third day of the disease, which began with **sore throat** and **vomiting** on the 9th.

Previous History.—Five of the same family were simultaneously sent to the hospital, on account of diphtheria, one of whom required tracheotomy for laryngeal diphtheria immediately on entrance.

On admission.—Exudation was observed in large quantity on **both tonsils**, on the **uvula**, and on the **soft palate**. Considerable **swelling** on both sides of the neck was also noted. *Temperature*, 99·4° ; *pulse*, 130. Intolerable fœtor of the breath.

The bacteriological examination demonstrated the presence of the bacillus diphtheriæ (long variety) in an almost pure cultivation (Fig. 25).

December 12th.—*Temperature*, 99·4° ; *pulse*, 128. The *urine* passed during the last twelve hours was 8 ounces, and contained only a trace of *albumen*. Bowels confined. Two pieces of membrane were shed, leaving a freely bleeding surface on the right

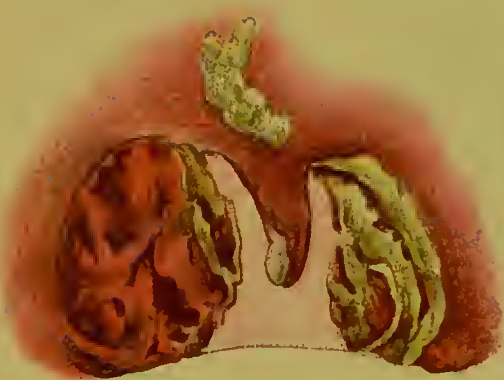

FIG. 24.

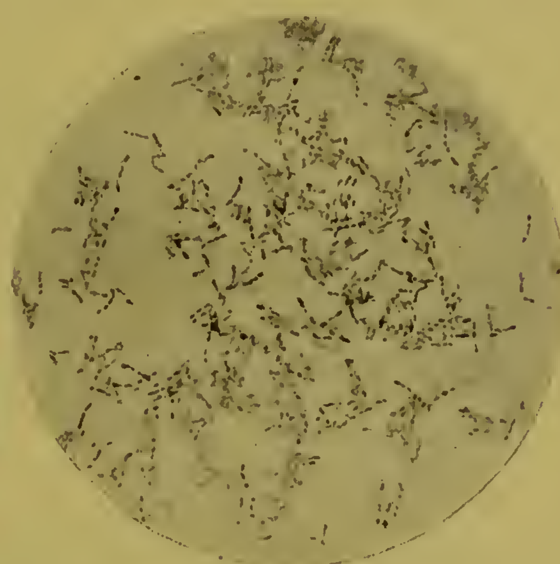

FIG. 25.

tonsil; the exudation which remained had a shrunken appearance (Fig. 24).

Membrane apparent in **both nostrils**. The fœtor continued. At night the *temperature* was 99·6° ; *pulse*, 120. A considerable mass of dirty-looking membrane still remained on the uvula, left tonsil, and palate, which continued to be hæmorrhagic ; some came away during the day. Copious sero-sanguineous discharge from the nostrils was observed ; but the fœtor was less.

December 13th.—*Temperature*, 99·4° ; *pulse*, 116. The *urine* passed in twenty-four hours was 19 ounces, and contained $\frac{1}{10}$th

albumen. *Bowels* confined. *Tongue* dry and blood-stained. The *fauces* were covered with dirty brown mucus, but only a small quantity of membrane was apparent.

December 14*th*.—*Temperature*, 99·2°; *pulse*, 108. The *urine* contained ¼ albumen, and the total quantity passed was 19 ounces in twenty-four hours. A thin layer of membrane was present on each tonsil. Marked reduction in the swelling of the lymphatic glands, nasal discharge, and fœtor have ceased.

December 16*th*.—A large ecchymosis is noticed on the abdomen over the site where the serum was injected. *Temperature*, 98·2°; *pulse*, 104.

December 19*th*.—*Temperature*, 98°; *pulse*, 100. The ecchymosis has nearly disappeared.

December 21*st*.—*Suppression* of urine since 6 P.M. on the previous evening. *Temperature*, 97·4°; almost pulseless at the wrist. Tongue dry and brown. Pupils contracted. Drowsy.

Death occurred at 5.10 P.M., no urine having been voided for the last twenty-three hours.

Treatment.—**Two injections** of **antitoxin** (**B. I. P. M.**) were given; one of 20 c.c. on December 11th, and a second 10 c.c. on December 12th. The fauces were painted with Loeffler's solution.

No autopsy permitted.

Case 3.—*Faucial exudation; recovery.*

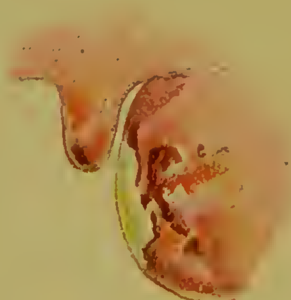

FIG. 26.

A female child, æt. 13, **admitted** *November* 18*th* with sore throat and vomiting which had occurred two days previously. Membrane was seen on the left tonsil and uvula, proved *bacterio-*

logically to be almost pure diphtheria. *Temperature*, 98°; *pulse*, 104. A trace of albumen discovered in the urine, which was free in quantity. Cervical glands on left side slightly enlarged.

November 25th.—Still membrane on left tonsil; characteristic raw surface, with hæmorrhagic and ulcerated spots on both tonsil and uvula, where the exudation has recently separated (Fig. 26). The child, who was **treated** with antiseptics locally and iron tonics internally, made a good recovery, with slight palatal paralysis.

Case 4.—*Lacunar diphtheria; recovery; tonsillotomy three months later; secondary exudation; attenuated bacillus; recovery.*

A man aged 25 years. Admitted to hospital on November 8th, 1894.

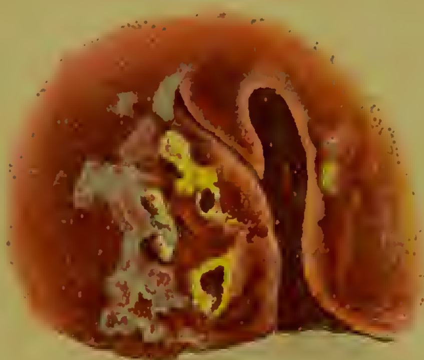

Fig. 27.

Previous History.—The patient had been subject to sore throat and had suffered from one attack of rheumatic fever. His residence was believed to be healthy, but a case of diphtheria had occurred in the house some years ago. The present illness began on the day before admission.

On admission the whole **fauces** were of a **deep red** colour, the **uvula**, which was long and inflamed, clinging to the **right tonsil** which was greatly enlarged, with an inflammatory thickening of the corresponding anterior pillar projecting as a somewhat flattened ridge-like tumour far beyond the middle line (Fig. 27). On its surface were several widely open and deep lacunæ, some covered with the ordinary yellow caseated secretion of acute lacunar

tonsillitis. Beyond this were several patches rather between than on the lacunar openings, of pellucid exudation not difficult to remove, nor when removed leaving a bleeding surface. The **left tonsil** was less enlarged and inflamed; it exhibited but one blocked crypt (Fig. 27).

The case presented all the clinical features of **Acute Lacunar Tonsillitis**, of a probably insanitary origin, in a patient the subject of chronic tonsillar hypertrophy.

A **culture** was made from the right tonsil. The swab went deeply into several large lacunæ, which appeared to confirm the

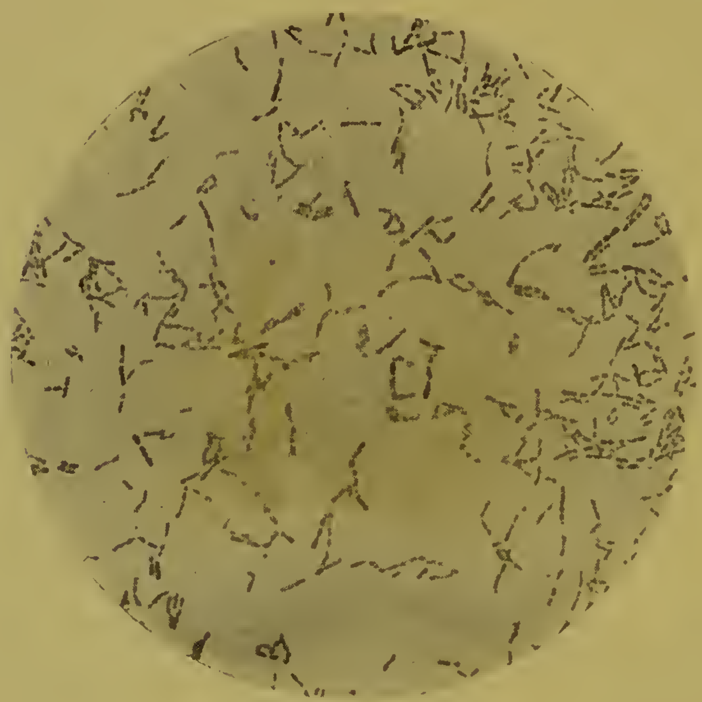

FIG. 28.

diagnosis at the bedside. The **bacteriological** report, however, demonstrated that the Klebs-Loeffler bacillus was present, the organism being of the long variety (Fig. 28). In the light of this report the case was taken as an example of lacunar diphtheria as first noted by Jacobi, but only recently confirmed bacteriologically by Koplik.

The *temperature* on admission was 101·8°; on the following day, November 9th, 101·8°; on November 10th, 101·4°; on November 11th, 100·4°. The pulse rate being, on the average, about 100.

The glands at each angle of the jaw were somewhat enlarged and tender for the first three days after admission to the hospital, but soon subsided.

On *November 13th* a marked change was observed in the appearance of the throat, which will be at once evident by reference to Fig. 29. Both tonsils were more enlarged, the fauces were of a livid purple colour, and covered with a tough and dirty yellow exudation—a coalescence, as it appeared, of the former separate secretions from the crypts. The pellicular membrane in the lacunar interspaces had disappeared. The palate generally was of a bright red colour, and there was now much less difficulty in accepting the

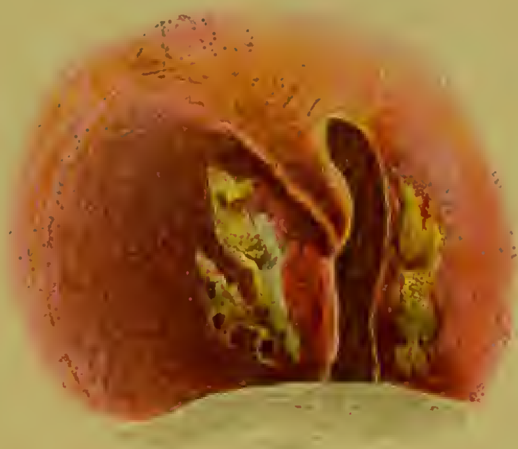

FIG. 29.

bacteriological diagnosis, albeit many of the characteristic physical signs and symptoms of a true diphtheria were absent.

The patient made a rapid and complete recovery, and **no paralytic sequelæ** *of any kind occurred.*

February 28th, 1895.—Three months after his discharge from hospital the patient presented himself on this day for treatment of his still hypertrophied tonsils, which were removed.

March 2nd.—A thin, whitish membrane was observed on the faucial wounds, the right tonsil, which had been cleanly removed, appearing to "fungate" (Fig. 30). On removal of a portion of the exudate fairly free bleeding followed.

A culture being made, a typical growth of the pseudo-bacillus of diphtheria in association with cocci, was obtained; the bacilli being short, stunted, and segmented, and showing the characteristics of the short variety of the microbe, frequently recognised in cultures from patients convalescing from diphtheria, and some-

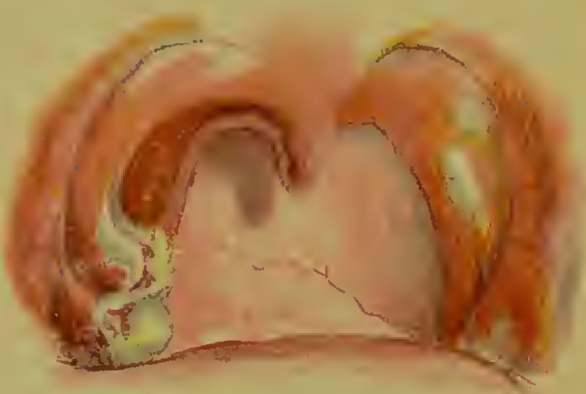

Fig. 30.

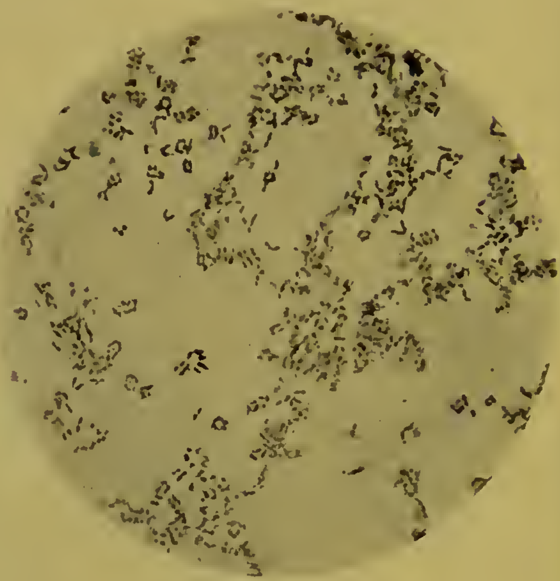

Fig. 31.

times vaguely described as "Involution" forms of the bacillus diphtheriæ (Fig. 31).

Further cultures failed to develop the bacilli, though the cocci multiplied in profusion.

The throat gradually cleared, and later swabbings did not reveal any evidence whatever of diphtheria bacilli.

CLASS II.

Bacillus Diphtheriæ with Streptococcus.

Case 5.—*Slight faucial exudation; acute cervical cellulitis; nasal diphtheria, probably post-scarlatinal; death.*

A female child, aged 3 years, admitted on November 3rd, 1894, on the eleventh day of the disease.

Previous History.—The child appeared to be very ill on October 22nd, the date on which her throat first became sore and inflamed; on the following day an erythematous rash was

observed on the trunk and limbs, and the next day both sides of the neck under the angles of the jaw were swollen and tender. Five weeks previously a sister 5 years old had been attacked with sore throat and discharge from the nose. No rash had been observed, and she had made a good recovery.

On admission.—The throat was inflamed. A thin film was seen on both sides of the fauces. There was a large dirty cavity in the right tonsil. Membrane was present in both nostrils. Both sides of the neck were extremely enlarged and inflamed, giving the *Cou proconsulaire* of the French, and resembling a

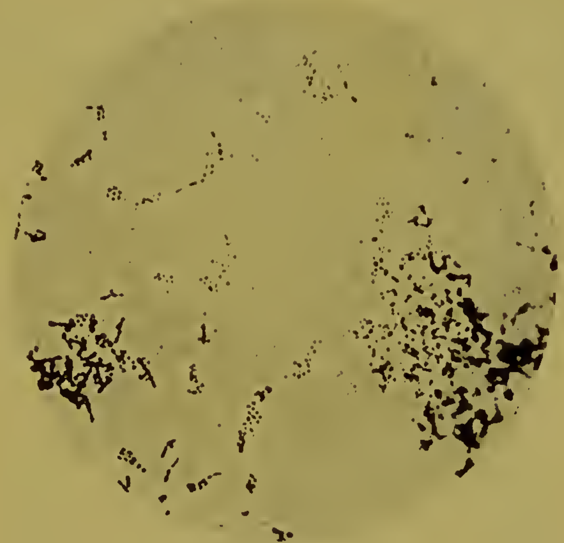

Fig. 32.

severe attack of *Angina Ludovici.* She was semi-delirious. The temperature was but 98°, and pulse 104.

The **bacteriological** examination showed profuse small colonies, which **microscopically** demonstrated the bacillus diphtheriæ in small numbers, associated with streptococci in chains of four or five segments, and of *Batallion* arrangement with numerous disjointed cocci, single and in pairs (Fig. 32).

November 4th.—Delirium persists. The urine contained a haze of albumen. *Temperature,* 100·4°; *pulse,* 106. Death occurred at noon.

Treatment.—Local antiseptics and douchings of the mouth, poultices, and stimulants.

Case 6.—*Severe nasal diphtheria, probably post-scarlatinal; death.* A male, aged 13 months, a brother of the patient whose case has just been described (*Case* 5). Admitted at the same time as his sister, on November 3rd. His mother stated that he had been subject to head-colds, and was a mouth-breather from his birth.

On admission.—*November 3rd.*—Very pale, and of waxy complexion. Profuse sero-sanguineous discharge from nostrils, in which membrane was seen. There was epistaxis on the right side, and several petechiæ were observed on the face. *Temperature*, 100·2°; *pulse*, 78.

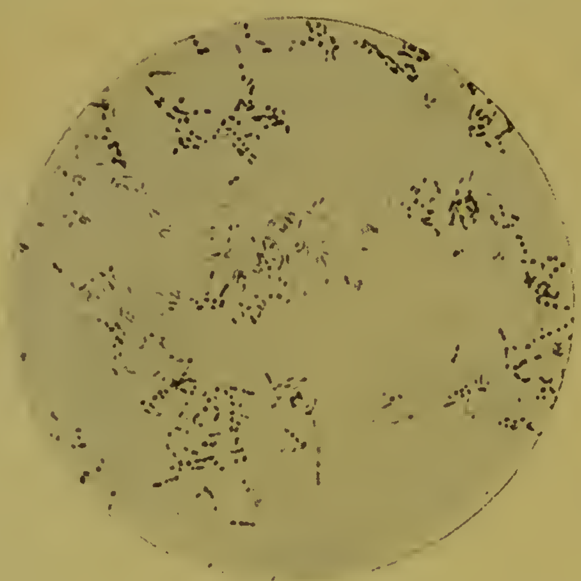

Fig. 33.

The **bacteriological** examination demonstrated profuse small colony growth of the diphtheria bacillus, a small form and a larger one staining markedly at both poles; associated with streptococci in chains of four or five elements, arranged in *batallion* form (Fig 33).

November 4th.—Almost moribund. *Temperature*, 99°; *pulse*, 82. Died, 7 P.M.

Treatment.—Antiseptic douches to both fauces and nares, with stimulants.

Case 7.—*Tonsillar exudation; adenitis; serum treatment; slight paralytic sequelæ; recovery.*

A female child, aged 6 years, admitted on *December 8th*, 1894. On the previous day was taken ill with sickness and sore throat, the neck being swollen on both sides. Has been a mouth-breather since birth.

On admission.—Both tonsils were enlarged and covered with membrane, the uvula being hidden by the swollen glands. Breath

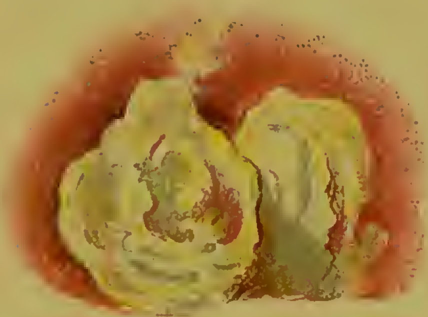

FIG. 34.

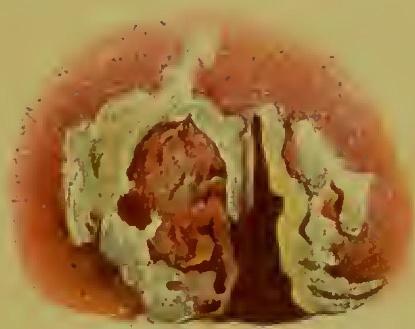

FIG. 35.

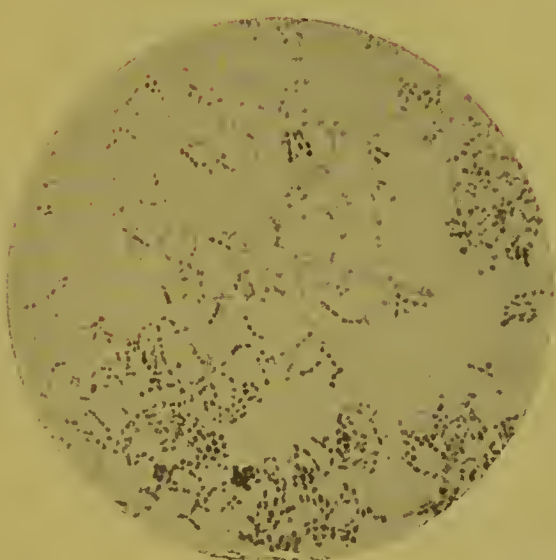

FIG. 36.

fœtid. Cervical glands on both sides enlarged (Fig. 34). *Temperature*, 98·4°; pulse, 100. Urine contained no albumen.

December 9th.—Slight cyanosis. Right tonsil still overlaps and hides uvula. The tissues bleed freely on attempting to remove membrane. Fœtor continues. Urine passed amounted to 34 oz. in twenty-four hours. No albumen. *Temperature*, 97·4°; *pulse*, 122.

The **bacteriological** examination demonstrated two main forms of growth, one white and discrete, the other semi-translucent. **Microscopically**, the bacillus diphtheriæ and streptococcus pyogenes were shown to be present (Fig 36).

December 10th.—Membrane whiter and rolling up at edges, separating at centre; fœtor continues. Complexion ashy and waxen. Restless, bowels confined. Glandular swelling subsided. Urine, 18 oz. in twenty-four hours. No albumen. *Temperature*, 100·4°; *pulse*, 136.

December 11th.—Right tonsil is still very large, the left one is smaller. The membrane is gradually separating, clearing, rolling off, so to speak. It is much whiter, much thinner, and more transparent. There is no fœtor. Urine passed, 18 oz., contains a trace of albumen. *Temperature*, 98·4°; *pulse*, 110.

December 13th.—Tonsils continue enlarged, covered with a layer of pultaceous secretion. The glands are shotty on the left side. Urine (19 oz. in twenty-four hours) contains a haze of albumen. *Temperature*, 97·4°: *pulse*, 108.

December 15th.—Membrane almost gone, except a slight portion on the right tonsil. Appetite good. *Temperature*, 98°; *pulse*, 100.

The child made a good recovery. Only slight paresis of the palate and ciliary muscles were observed; these soon disappeared.

Treatment.—One injection of **antitoxin** (**B. I. P. M.**), 20 c.c., was given on December 9th, and the usual antiseptic swabbings and douches were employed. Later, nervine tonics for the sequelæ.

Case 8.—*Faucial and nasal exudation; adenitis; serum treatment; anuria; recovery.*

A female child, aged 6 years. Admitted *December 11th*, 1894.

Previous History.—The patient was the sister of the little boy referred to in Case 2, and was removed to the hospital on the same day. All the children at their home, six in number, slept in the same room. On December 9th the patient was taken ill with sore throat and vomiting.

On admission.—Neck was swollen on both sides, and very painful.

Large masses of membrane were seen on both tonsils, which were very swollen and completely concealed the uvula. Membrane also diagnosed in post-nasal space. *Temperature*, 98·4°; *pulse*, 128.

The **bacteriological** report stated that, on culture, colonies of the bacillus diphtheriæ were evident, and microscopically the presence of the diphtheria bacillus associated with streptococcus pyogenes was demonstrated.

December 12*th*.—A large mass, over 3 inches long and 2 inches in circumference, was removed with forceps from the nares. No hæmorrhage followed. Later in the day the membrane was seen to be separating from the fauces, crackling away as it were, but the uvula which is now visible is seen to be very thickened, covered with exudation (Fig. 37). Membrane seen in nostrils. Urine

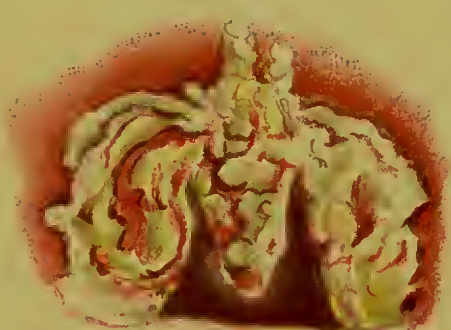

Fig. 37.

passed was 6 oz. in twelve hours; it contained a heavy trace of albumen. *Temperature*, 98·4°; *pulse*, 120.

December 13*th*.—The right tonsil presents a red and almost raw appearance, the membrane has almost gone except a thin layer on the left tonsil. The uvula is large and covered with membrane which is separating and leaving spots of exposed mucous membrane. The glands are still slightly enlarged, especially on the left side. Eleven oz. of urine passed in twelve hours. *Temperature*, 98·4°; *pulse*, 108.

December 15*th*.—Throat nearly clear of membrane. Thirty oz. of urine passed in twenty-four hours; a trace of albumen. Tongue clean. Food taken well. Patient very bright and cheerful. *Temperature*, 98·4°; *pulse*, 108. She made a very slow recovery,

being subject for many weeks to paroxysms of cardiac weakness with marked cyanosis.

Treatment.—One injection of 20 c.c. of **antitoxin** (**B. I. P. M.**), and the usual local antiseptic applications.

CLASS III.

Bacillus Diphtheriæ, with Strepto- and Staphylococcus.

Case 9.—*Tonsillar exudation, with ulceration; probably scarlatinal; recovery.*

A male child, aged 6 years. Admitted to hospital on *November 10th*, 1894, having suffered from sore throat since October 28th.

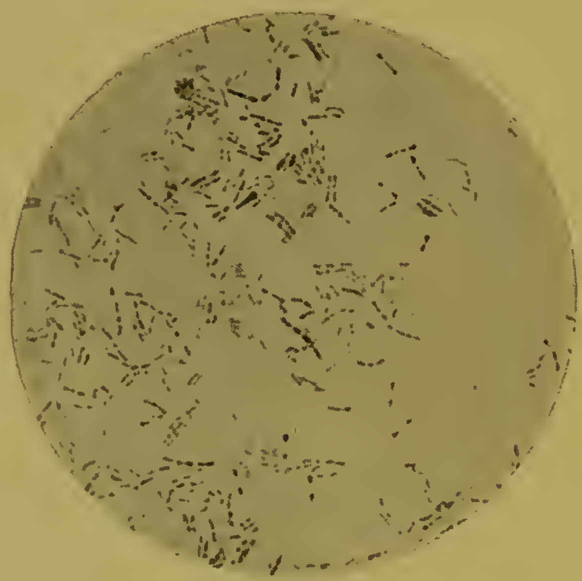

Fig. 38.

On admission.—His countenance was puffy, and rather characteristic of scarlet fever; but no distinct history could be ascertained of a rash, nor of peeling. Skin was dry, and *temperature* 99° F. The fauces were seen to be inflamed and dirty-looking. An excavated and exudation-covered ulcer was seen on the right tonsil; there was slight enlargement of the glands on each side of the neck. These could be felt as separate small nodules and were not quite typical of the adenitis of diphtheria. Albumen was present in the urine to the amount of $\frac{1}{10}$th.

Bacteriological examination showed colonies containing a few bacilli of diphtheria; the main mass consisted of strepto- and staphylococci.

The photo-micrograph (Fig. 38) shows but few of the associated cocci, due to inadvertence in selection from the slide of the exhibited area.

The patient recovered.

Treatment.—Antiseptic swabbing, and douches. Iron and chlorate of potash mixture given internally.

Case 10.—*Faucial and nasal exudation; tendency to hæmorrhagic form; cervical adenitis; serum treatment; anuria; death.*

A male child, aged 6 years, admitted *December 26th*, 1894. The history was that he was taken ill on December 23rd, the initial symptoms being sore throat and vomiting.

On admission.—There was extensive exudation on both tonsils, uvula, and soft palate. The tonsils were very large, and bled readily when touched. Both nostrils were blocked with membrane, and there was profuse nasal discharge, accompanied by great fœtor. The neck was much swollen on both sides. The complexion was grey and earthy-looking. The urine, of which 14 oz. was passed in the first twelve hours, contained much albumen. *Temperature*, 99·8°; *pulse*, 136.

Bacteriological examination demonstrated the presence of the bacillus of diphtheria in association with streptococcus pyogenes, staphylococcus, and other bacteria.

December 27th.—No urine passed for nine hours. Patient very restless, breathing laboured. Lips and tongue very dry. Throat condition remains the same as yesterday. *Temperature*, 100·2°; *pulse*, 156.

At 8 p.m. almost pulseless. A very small quantity of urine was passed in bed. Death occurred at 9.15 p.m.

Treatment.—Two injections of **antitoxin (B. I. P. M.)**, one of 10 c.c.; the second 8 c.c. of Behring's; diuretic mixture, antiseptics, &c.

Case 11.—*Faucial, post-nasal, and laryngeal exudation; serum treatment; anuria; death.*

A male child, aged 3 years, was admitted to hospital on *December 8th*, 1894, having suffered from a sore throat since December 3rd, followed by swelling of the cervical glands on December 6th.

On admission.—Membrane was seen on the left tonsil, extending somewhat to the soft palate. There was also a small piece observed on the right side of the uvula (Fig. 39). On turning up the tip of the latter, membrane was seen on the posterior surface,

Fig. 39.

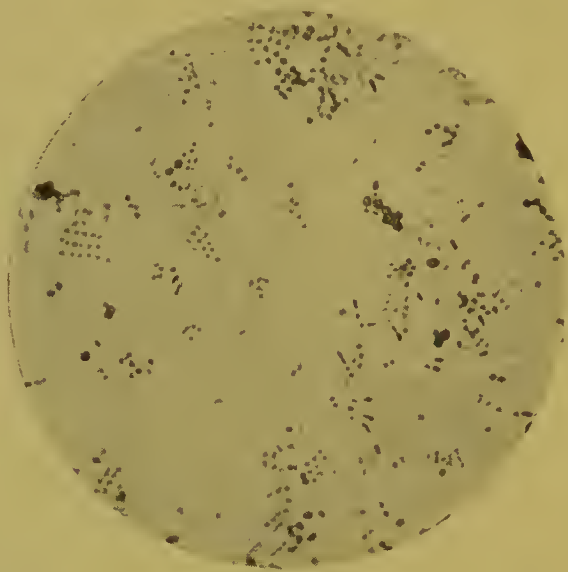

Fig. 40.

and with the laryngeal mirror, on the tip of the epiglottis. The *temperature* was 97·8°; *pulse* 100.

December 9th.—The face was puffy. A vesicular eruption resembling that of acute eczema was observed under the angle of the right jaw. *Temperature*, 97·8°; *pulse*, 100.

Bacteriological examination showed a profuse growth, evidently composed of several organisms, most prominently streptococci and staphylococci. **Microscopically**, staphylococcus, albus and aureus, diplococcus, streptococcus (of marked batallion arrangement), and bacilli resembling the so-called "involution forms" of the bacillus diphtheriæ were demonstrated (Fig. 40).

Note.—It is believed that the usual precaution against making a culture within reasonable time of employing antiseptics was overlooked in this case. Hence the unsatisfactory character of the report as to the bacilli.

December 10*th.*—No urine passed for nine hours; but, from the state of the sheets, some was believed to have been voided during the night. The eruption has disappeared. The face is not so puffy. Very restless, little or no sleep during the past twelve hours. No urine passed for eighteen hours. *Temperature,* 97·8° F; *pulse,* 136. Died at 7 P.M. in the evening.

Treatment.—Antitoxin (B. I. P. M.) 10 c.c. Local antiseptic, swabbing, and douching.

Case 12.—*Diphtheria without exudation on fauces, and with negative diagnosis of bacilli; Otorrhœa on twelfth day, with presence of bacillus; serum treatment; recovery.*

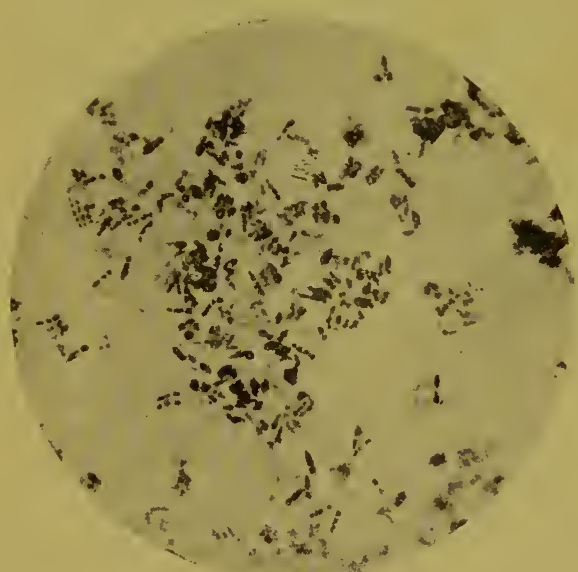

FIG. 41.

A female child, aged 2 years, admitted to hospital on *January* 23*rd,* 1895, on the third day of the disease.

On admission.—No membrane was observed in the throat, nor was any present during her residence in the hospital. The tonsils were large and the neck swollen. *Temperature,* 102°.

The **bacteriological** report was negative, no diphtheria bacilli being demonstrated. The only organisms present were strepto- and staphylococci.

10 c.c. of **antitoxin** (**B. I. P. M.**) were administered, and the temperature, after a slight rise, fell to 101° F.

February 4th, the twelfth day after admission, after a slight rise of temperature, a muco-purulent discharge was noted from the right ear; not painful.

February 6th.—A similar discharge was present in the left ear; without any pain inside or outside the meatus. A culture was made from the otorrhœal discharge on the first day, before any local treatment of the discharge was commenced.

The **bacteriological examination** demonstrated diffuse, greyish-white colonies, with a few points of a lighter colour. Microscopically, the presence of the bacillus diphtheriæ, associated with strepto- and staphylococci, was detected. The patient made a good recovery, but developed palatal and ciliary paralysis.

February 11th.—*Temperature*, 100·8°. Some adenitis.

March 21st.—A haze of albumen for twenty-four hours.

March 25th.—Palatal paralysis.

Treatment was chiefly directed to irrigating the throat, and, later, syringing the ears with boracic acid lotion. One injection of 10 c.c. of **antitoxin** (**B. I. P. M.**) was given on the day of admission.

CLASS IV.

Bacillus Diphtheriæ, with Streptococcus and Diplococcus.

Case 13.—*Fourth attack of diphtheria; tonsillar exudation; recovery, with grave paralysis.*

A female aged 40. Admitted to hospital *October 31st*, 1894.

Previous History.—The subject of chronic albuminuria. She had been for eight years a nurse in an infectious fever hospital, and during the last three years, including the present occasion, had been attacked four times with diphtheria. One of her pre-

vious attacks of diphtheria was followed by slight paresis and diplopia.

On admission.—Membrane was present on both tonsils. There was slight glandular enlargement. *Temperature,* 100·4°; *pulse,* 88.

November 4th.—The condition of the throat was characterised by extreme anæmia, except at the parts attacked. There was thickening of the fauces, and the pillars of the tonsils were merged—as often seen at this period in the life of a patient who has been the subject of chronic tonsillar hypertrophy.

There was only one small thin pellicle of membrane on the

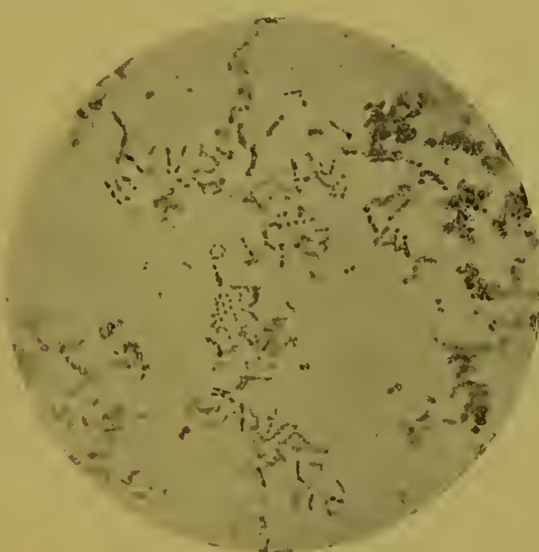

Fig. 42.

right tonsil, and this was completely removed by the swab, and was the source of the culture.

The **bacteriological report** was that the culture showed a profuse growth of small heaped-up colonies; the bacillus diphtheriæ was present, associated with streptococcus and diplococcus (Fig. 42).

November 5th.—No membrane to be seen. The temperature was subnormal, and the urine contained about $\frac{1}{20}$th albumen.

November 11th.—The palate and fauces were very anæmic. Temperature subnormal. Urine contained a heavy haze of albumen.

November 15th.—Patient complained of pain in both legs, and on examination the knee jerks were found to be slightly exaggerated.

November 25th.—Some loss of power in left hand and arm; knee jerks exaggerated; she has some difficulty in walking, and drags her feet. Some diplopia noted. No albumen in the urine. For a few days past the patient has been assisting in nursing scarlet fever cases.

It suggested itself to us that, as the patient was engaged in the wards, the micro-organisms were constant inhabitants of her throat, but the probability of such an hypothesis was disproved by a culture taken on November 26th, at the end of the fourth week of her attack.

The **bacteriological report** of this later culture was that no definite growth of any sort could be seen, and under the microscope only a few micrococci of indefinite character were observed. The case, therefore, appears—as far as the fourth attack is concerned—to be one of genuine re-infection. We may add that already grave paralysis of limbs and sight are supervening.

November 30th.—The loss of power in the left arm and in both legs still remains; diplopia continues. The urine contains nearly $\frac{1}{4}$th albumen.

The patient was subsequently superannuated, the paralysis not having disappeared at the time she left the hospital.

Remarks.—It is sufficient to note the bacteriological confirmation of the clinical diagnosis of a fourth attack of true diphtheria in one individual, and at such frequent intervals.

Her chronic kidney disease and night duty were probably exciting factors, and as the after history proves, paralytic symptoms have supervened, which leaves no clinical doubt as to the nature of the case. Another point of interest is that here is a case in which recovery from diphtheria has four times taken place in a very unpromising subject, and in that complication of diphtheria characterised by the presence of both the Klebs-Loeffler bacillus and streptococcus, said by some authors to be invariably fatal, and recorded in the clinique of Roux as having been fatal in thirteen out of fourteen cases.

CLASS V.

Bacillus Diphtheriæ and Diplococcus.

Case 14.—*Abundant tonsillar deposit; paralytic sequelæ; recovery.*

A female child, aged 5 years, admitted to hospital *November 10th*, 1894. The parents stated that the patient was taken ill on November 7th with sore throat. There was no sickness, and no cutaneous rash had been observed.

On admission.—The throat was very inflamed, with a thick

Fig. 43.

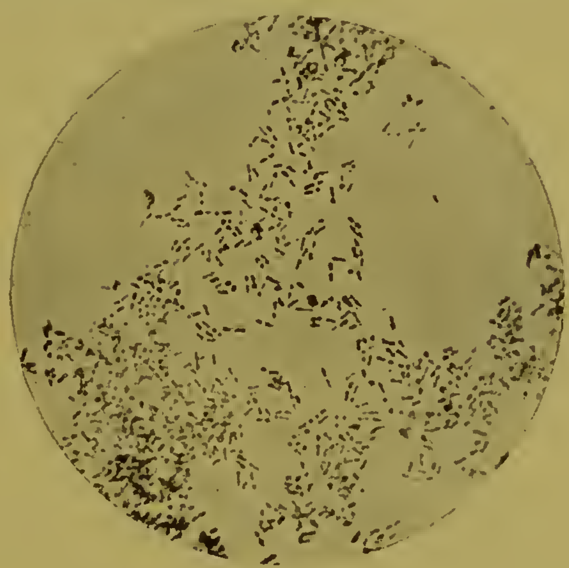

Fig. 44.

plaster of deposit of membrane on both tonsils; the uvula being unaffected (Fig. 43).

The skin was very dry. A haze of albumen was present in the urine. *Temperature*, 98° F.

Bacteriological examination demonstrated numerous small colonies of a milky white growth.

Microscopically, the bacillus diphtheriæ was shown to be present in great abundance, with some diplococci (Fig. 44), only a few other organisms being visible.

November 12th.—The cervical glands were enlarged on both sides.

The exudation was thinner, and of a pearly colour; the throat was less inflamed. *Temperature*, 100·4°.

November 14th.—The membrane was still present in very pellucid patches on the tonsils. *Temperature*, 101°.

November 25th.—The child doing very well, and her general condition very satisfactory. Membrane, however, still present on the left tonsil, and on the right anterior pillar of the fauces. It has a dirty appearance, unlike the pearly tint formerly observed. The cervical glands are still slightly enlarged, and the urine contains a trace of albumen. *Temperature*, 98·4°.

December 9th.—Throat quite clear of membrane. The patient has had strabismus and diplopia for the last four days. She eventually made a good recovery.

Treatment.—Antiseptic swabbings of the fauces, syringing the throat with boracic acid lotion. Iron and chlorate of potash internally.

CLASS VI.

Streptococcus.

Case 15.—*Pseudo-diphtheria of scarlatinal origin; recovery.*

A female, aged 29 years. Admitted to hospital on *October 15th*, 1894, seven days after the initial symptoms occurred.

Previous History.—On October 8th she was taken ill, the first symptom being severe headache, followed by severe sickness and diarrhœa.

On admission.—The throat was inflamed and membrane seen on both tonsils. The urine contained a trace of albumen. *Temperature*, 104·6°; *pulse*, small, 112.

October 27th.—Desquamation commenced. The urine still contained a trace of albumen.

October 29th.—Desquamation general all over the body.

November 4th.—Some membrane was observed on the left tonsil (a second manifestation). On removal of a portion of this exudation, a slight trace of hæmorrhage occurred.

Bacteriological examination showed an almost pure cultivation of streptococcus, which microscopically appeared to be arranged in flexuous chains, consisting of from four to eight elements (Fig. 45).

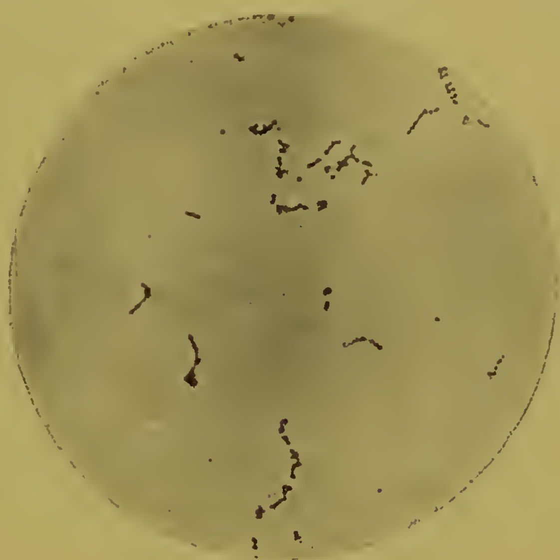

Fig. 45

Treatment.—Baths, and inunction of eucalyptus oil to the cutaneous surfaces during the period of desquamation; antiseptic gargles to the throat; diuretics internally.

The patient recovered without any paralytic or renal sequelæ.

Case 16.—*Pseudo-diphtheria of probably scarlatinal origin; recovery.*

A female, æt. 10½, who was attacked with sore throat on *November 2nd*, 1894.

The neck and glands under the jaw became swollen on November 5th, and she was **admitted** into hospital on *November 11th.* The throat manifestations consisted of inflammation, deeply excavated and vertically parallel ulcers of the tonsils, with dirty greyish and pultaceous patches on the surfaces. The uvula was red, with slightly opalescent exudation on the left side (Fig. 46). Sub-maxillary and cervical adenomata. *Temperature,* 99°. Urine exhibiting haze of albumen.

Although there was no history of a rash, the case in many

respects was one of scarlet fever. The diagnosis was *pseudo-diphtheria.* A culture was made on November 13th, and the following was the report of the **bacteriological examination** :—

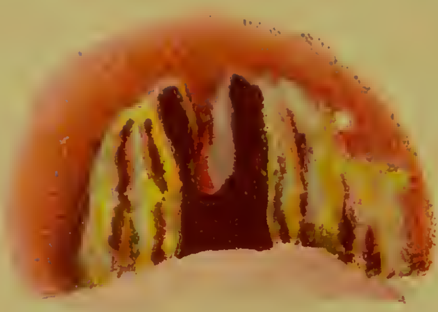

Fig. 46.

Fig. 47. (Drawing.)

The growth consists entirely of streptococcus, and, as the drawing shows, in long flexuous chains (Fig. 47).

Treatment. — Local antiseptic douches ; chlorate of potash confection, and iron internally.

A good recovery was made.

CLASS VII.

Streptococcus and Diplococcus.

Case 17.—*Pseudo-diphtheria, and peritonsillitis of insanitary origin ; recovery.*

A male, æt. 42. **Admitted** on *November 5th,* on account of a sore throat, from which he had been suffering for twenty-four hours, with general malaise.

There was a *cloudy,* almost membranous, appearance of the fauces, which were much thickened and covered with a creamy secretion. There was also inflammation of both tonsils, which were not enlarged. The soft palate and uvula were also inflamed,

the latter being œdematous and translucent. *Temperature,* 100° F.; *pulse,* 110.

The diagnosis was that of *insanitary faucitis* and *peritonsillitis.* A culture was made from the tonsils, and the **bacteriological report** proved the presence of *streptococci* and a few *diplococci.* In

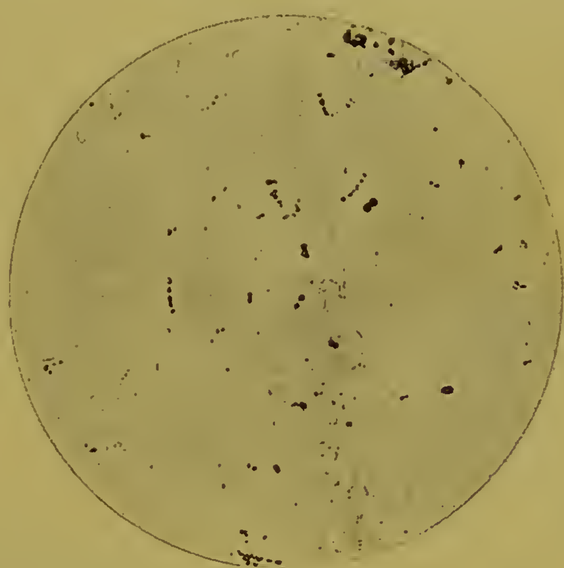

FIG. 48.

this case the streptococci were of the short, rigid, or least virulent variety (Fig. 48).

Treatment.—A mixture of mercuric biniodide, and carbolic gargle.

Good recovery.

CLASS VIII.

STAPHYLOCOCCUS.

Case 18.—*Pseudo-diphtheria accompanying typhoid fever; death.*

A male, æt. 27, who was taken ill nine days before admission, with pain in the back and sore throat. He was **admitted** on *November 5th* with notification of diphtheria, with membrane on the uvula and tonsils. *Temperature,* 101·4°. Enteric spots were discovered on the abdomen, and he passed typhoid stools. Between November 5th and November 11th the temperature rose to 106°. The fauces and uvula were of a deep red colour and

covered with membrane, especially on the right side up to the junction with the palate.

From a culture made on November 11th, the following was the **bacteriological report**:—Numerous yellowish white colonies, tending to coalesce and form streaks.

Microscopic examination showed an almost pure specimen of staphylococci, with a few cocci arranged in pairs, and a few bacilli, probably *not* those of diphtheria. Independently of the fact that there were no colonies resembling those of the Klebs-Loeffler organism to be seen in the culture tube, the bacilli in the slides were much smaller than those of diphtheria.

The patient died on November 13th from collapse following on perforation of the bowel.

Case 19.—*Pseudo-diphtheria; exudation on fauces and uvula; recovery.*

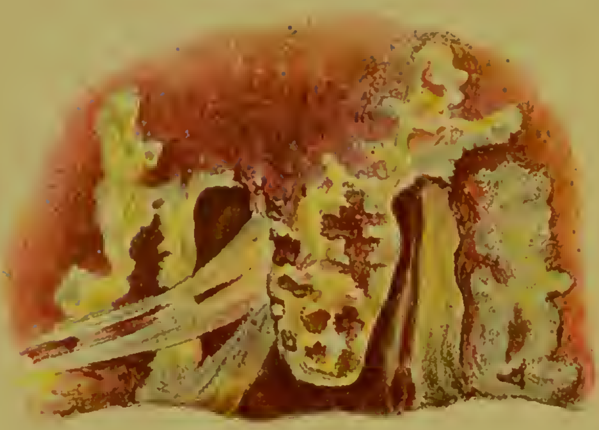

Fig. 49.

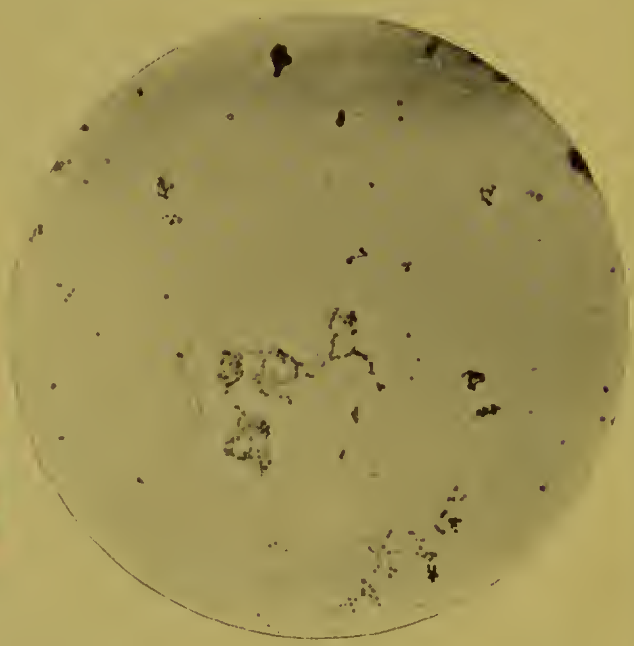

Fig. 50.

A female, æt. 40, who was taken ill with sore throat on November 17th, 1894, vomiting on November 18th, and was **admitted** into hospital on *November 24th.* On *November 25th* the fauces and uvula were seen to be much swollen; dirty exudation patches more or less confluent were observed on the right

tonsil which was deeply excavated, lighter coloured patches were observed on the left tonsil, and several yellow ones on an almost œdematous uvula. A curious feature in the throat appearance was a quantity of viscid mucus, not only in the post-nasal space, but extending from the palate across to the tonsil, forming ropy bands (Fig. 49). Several portions of membrane of unusually thin and transparent consistence had been coughed up; notwithstanding that albumen was present in the urine to the extent of one-eighth, it was difficult to recognise this case as one of typical diphtheria.

A culture was taken on *November 25th*, and rather more than usual force was employed to obtain a full quantity of secretion, but, nevertheless, there was no hæmorrhage, nor evidence of ulceration on the surface whence the exudate was taken.

The **bacteriological report** was as follows:—The culture shows a few whitish-yellow colonies. **Microscopic** examination demonstrates these to consist of almost pure growth of staphylococcus (Fig. 50). On *November 30th* the throat was practically clear, the larynx normal, and the vocal cords white.

Treatment.—Perchloride syringing, application of Loeffler's solution, and salines internally.

Case 20.—*Pseudo-diphtheria, with sparse non-virulent bacilli; recovery.*

A female, aged 22, occupied as an infirmary nurse. First fell ill on March 31st, 1895. **Admitted** *April 5th*, complaining of extreme pain in throat on attempting to open the mouth. **On examination,** the tonsils were observed to be much swollen, with a rather inflamed and sloughy patch on the right one, and with a blocked lacuna on the left. The uvula inflamed and œdematous. There was much mucus clinging about the fauces, but no exudation on the back of the pharynx. There was no glandular enlargement. *Temperature*, 101° F. Albumen a haze. 15 c.c. **antitoxin (B. I. P. M.)** injected.

April 7th.—*Temperature*, 100° F. A considerable amount of membrane was coughed up, which was very thin and semi-trans-

parent in character, very similar to that in the last case, and mixed up with thick viscid mucus. On the clinical evidences the diagnosis was **insanitary tonsillitis,** probably due to staphylococcus. Two cultures, one from the throat and one from this discharged exudate, resulted in a **bacteriological report** to the

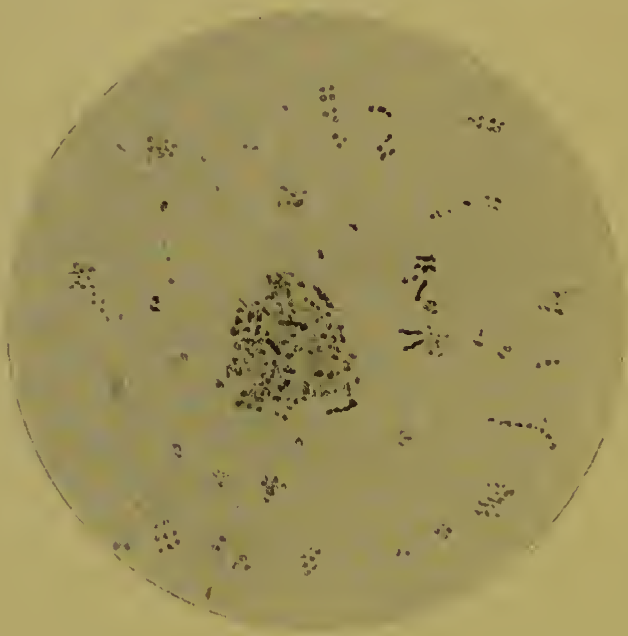

Fig. 51.

effect that there were large quantities of staphylococci, with a very few short, stunted bacilli of diphtheria. A twice repeated examination in another laboratory failed to find bacilli at all. The patient made a good recovery, without paralyses.

CLASS IX.

Staphylococcus and Diplococcus.

Case 21.—*Pseudo-diphtheria of tonsils and uvula ; recovery.*

A man, æt. 21. **Admitted** and seen as out-patient, *November 5th,* 1894, for sore throat, from which he had suffered for twenty-four hours. The throat manifestations were considerable swelling and inflammation of both tonsils, with a sort of pellucid muco-membranous exudation. The inflammation extended to the

anterior pillars of the fauces, soft palate and uvula, which was œdematous and translucent. The diagnosis was insanitary faucitis and peri-tonsillitis. A culture was made, and the bacteriological

Fig. 52.

report was "sparsely scattered yellowish colonies, consisting of staphylococci, and cocci arranged in pairs" (Fig. 52).

Treatment by mercuric biniodide mixture and carbolic acid gargle. Application of Loeffler's solution.

CLASS X.

Diplococcus.

Case 22.—*Pseudo-diphtheria in acute lacunar tonsillitis; recovery.* A female, æt. 15 years. She had suffered from sore throat three days previous to admission as an out-patient on *November 5th.* The tonsils were enormously inflamed and enlarged, the crypts blocked with thick yellow caseous secretion, some confluent, and with a certain amount of opalescent cloudiness in the interspaces.

My diagnosis was *acute lacunar tonsillitis,* but in view that Jacobi has stated that many of these cases represent a variety of

true diphtheria, this was thought to be a good test case. A culture was therefore made.

The **bacteriological report** stated that no growth was visible to the naked eye, but the microscope showed the presence of a few cocci arranged as streptococci, mostly of the short and rigid

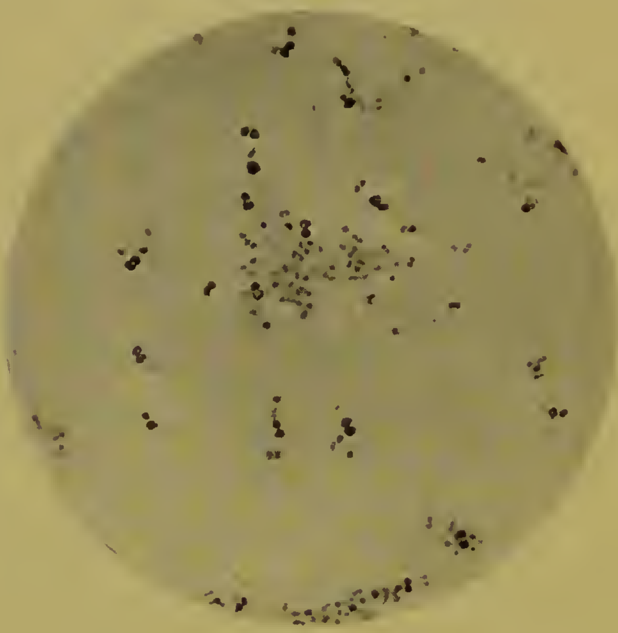

FIG. 53.

variety, the preponderance of the organisms being diplococci (Fig. 53). The tonsil suppurated and was incised. The case was long in clearing up, but recovery was complete.

Treatment.—Salicylate and chlorate of sodium mixture and carbolic gargle. Local application of Loeffler's solution.

CLASS XI.

DIPLOCOCCUS AND MYCELIUM.

Case 23.—*Pseudo-diphtheria in an advanced alcoholic, notified as diphtheria; death.*

A male, æt. 52, was taken ill with pain in the back and limbs and sore throat on *November* 1*st*, 1894. He was **admitted** on *November 3rd*. There was an erythematous rash on the legs and feet. Patches of greyish exudation were seen on the fauces, uvula,

right side of the soft palate, and on the left tonsil. Beyond this the throat generally exhibited several mottled patches of an almost purple colour, not unlike the skin eruption, on an unduly anæmic foundation (Fig. 54). With the *laryngoscope,* the epiglottis was seen to be inflamed and much thickened, while there was a thick patch of pale yellow secretion on its under surface, blocking up the vestibule, and hiding the vocal cords.

The case was sent to the hospital as one of diphtheria, but our diagnosis was surrounded with doubt; the balance of opinion was at first in favour of its being syphilitic, notwithstanding that the history rather negatived such a conclusion, and that there were no scars on the penis or in the groin. The man, however, was a

Fig. 54.

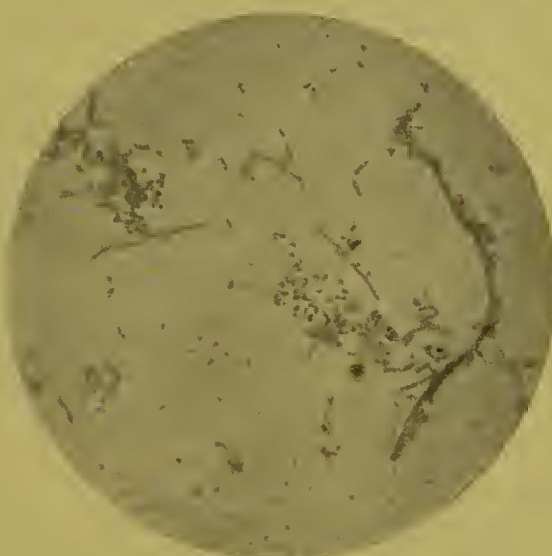

Fig. 55.

chronic alcoholic, had suffered from empyema of the left pleura, and was the subject of disease of liver, kidney, and heart. He died within forty-eight hours of admission, the patch on the right tonsil having in the meantime developed into an ulcer. Autopsy confirmed disease in all the organs named.

A culture was taken on *November 4th,* and the report of the bacteriological examination demonstrated the presence of "cocci in pairs, small bacilli in chains, larger than bacillus diphtheriæ. Large thick bacilli in chains, and fragments of a large fungus"

(Fig. 55). This case would appear to be removed from the field of diphtheria, but should still be classified as one of blood poisoning, in a subject suffering from extreme constitutional debility.

CLASS XII.

Indeterminate.

Case 24.—*Lacunar tonsillitis, with adenoids and reflex laryngeal cough; recovery.*

A male child, æt. 4. **Admitted** *November 3rd*, 1894, with a brassy, croupy cough, for which he was placed in the steam-tent and ordered syrup of chloral and ipecacuanha. On November 4th the cough was already better. This child had enormous tonsils, which almost over-rode each other, and on them were numerous

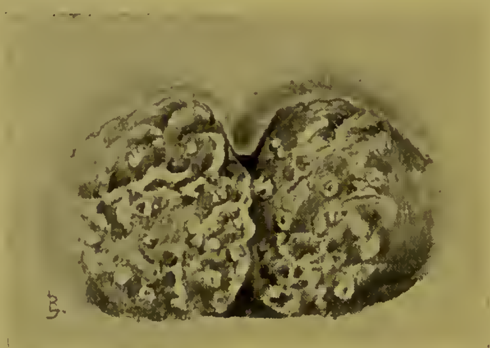

Fig. 56.

isolated patches of white secretion, which appeared to exude from lacunar orifices.

Our diagnosis was *acute lacunar tonsillitis* probably associated with hypertrophy of the pharyngeal tonsil, and that the cough and laryngeal symptoms were due to reflex spasm.

The **bacteriological examination** showed sparse, translucent colonies,—doubtful diphtheria.

The microscopic examination demonstrated:—

(1) Large bacilli in chains.

(2) Cocci arranged as diplococci.

(3) Smaller bacilli arranged in chains; these probably are not bacillus diphtheriæ.

A second culture was made, and the **bacteriological report** was as follows :—A sparsely scattered punctiform growth.

Microscopically, the growth showed (1) Cocci arranged as diplococci; (2) Small bacilli occasionally arranged in chains of two or three elements (the coliform bacillus of Roux?); (3) Large organisms, which seemed to be spores, possibly of the large bacilli.

No bacilli of diphtheria were present.

After History.—Although there was a trace of albumen in the urine, the child made a complete recovery, without any evidence of paralytic sequelæ. When discharged the tonsils were the same size as when admitted; the cough continuing, though not in such severe paroxysms.

CHAPTER IX.

THE ELEMENTS OF PROGNOSIS IN DIPHTHERIA.

THE forecast of diphtheria or of any of its congeners must always be very grave, and notwithstanding that many recoveries take place, complications are so numerous and serious that it is almost impossible to predict a successful issue from any attack, however mild at its commencement, until the patient is finally dismissed by the practitioner.

The elements of prognosis are indeed so variable in date of occurrence, and so diverse in their manifestations, that it is not possible to paint a clinical picture of diphtheria from the two-fold aspect of a favourable prognosis and the opposite, as was the fashion with the old masters of our science, and might still be done of many maladies whose march is in even and regular steps, with appointed dates for definite occurrences in its course. The only way to produce a picture of this character of diphtheria which could convey any sort of an idea of its various moods and phases would be by some process analogous to the present fashion of what is called "composite photography," in which the features of the same individual at various ages are printed one over the other, or by a superposition of the portraits of a number of different individuals, so as to produce a certain harmony of resemblances and a toning of differences. Too often such a portrait is robbed of all character, having lost the force of the strong and emphasised the feebleness of the weak; and so it would be in any such attempt at word-painting of the course of a diphtheria, though there would always remain stamped upon the portrait one special and uniform characteristic of the malady—namely,

Asthenia; for, as will be seen, each element of prognosis has to be considered mainly in relation to the prostrating effect of the diphtherial toxines on the respective vital functions of the individual.

The elements of prognosis may be divided under the following heads:—

(1.) What may be learned from the bacteriological examination.

(2.) What we learn from the history and surroundings of the patient, and what we acquire by direct observation on first seeing the case.

(3.) Complications of the vital functions during the course of the disease.

(4.) The sequelæ.

1. Bacteriological Prognosis.

The first point is to determine whether the case is one of true or pseudo-diphtheria; and there is no warrant for doubting that the test of distinctions is the presence or absence of the Klebs-Loeffler bacillus. As to the virulence of the bacillus, although personally we have no great confidence in a prognosis formed mainly on its length or calibre, the character of the rods must be taken into some account in this connection. The next element of prognosis consists in that formed by the association of the bacillus diphtheriæ, with one or more of the various cocci which have been shown to exert so definite an influence on the character of the malady. Should the case prove not to be one of true diphtheria, then the nature of the cocci which predominate must be taken into consideration, and the indications given by their variety, quantity, and arrangement, will require due interpretation.

If these points were observed, we should be in a position, not only to obtain more accurate data for prognosis, but we could on this basis construct a more scientific terminology than at present obtains, as has been more than once suggested in the previous pages.

Thus, instead of dividing diphtheria into *mild, grave, malignant, gangrenous*, &c., the terms which have hitherto been recognised, but which, in more than one instance in our present knowledge, might indicate a pseudo-diphtherial origin such as scarlet fever, we should speak of *bacillary, cocco-bacillary, coccal*, &c., with a prefix indicating the different kinds of non-bacillary micro-organism, and by this nomenclature we could indicate and be able to form a trustworthy and expressive diagnosis and prognosis at an early stage of the attack.

To return to the bacteriological forecast: if we find the diphtheria bacillus to be present, we must be prepared against those special results now known to be caused by the diphtherial toxines; and we must take precautions against a fatal result from cardio-respiratory paralysis and other acknowledged evidences of purely toxic origin. We are likewise in a position to give more heed to an early appearance of albumen in the urine than we should if the case were determined to be of a non-bacillary nature.

The less the diphtheria bacillus is associated with other micro-organisms the more favourable is the prognosis.

Most authorities are agreed that **Streptococci** are not only the most common of the associated organisms, but are also of the gravest omen, being responsible for infectious complications often of a most malignant character. Our own cases show that this organism, when associated with the diphtheria bacillus, is mainly of the "**batallion**" arrangement, and when it is present alone, in its "**flexuous**" form—which is the second in degree of virulence—gives us warning of an exanthematous origin or association; whereas, in its "**rigid**" form, it is comparatively inert. To revert to streptococcal association with the diphtheria bacillus: we may predict, if not already present, enlarged submaxillary and parotid glands, constituting the "proconsular neck" of French authors; rapid phlegmonous inflammation, and suppuration of glands and tissues; broncho-pneumonia, nephritis, and other complications of a septic nature, which will have either a fatal result or will materially retard the

recovery. When the streptococci are so numerous as to almost swamp the bacillus, the prognosis becomes all the more grave.

Staphylococci are often seen in association with the bacillus and streptococci, but may also frequently constitute a separate association with the diphtheria bacillus. In association with the specific bacillus, they are of less grave significance than streptococci, but being present in all cases where pus-formation is a symptom, their presence should lead us to expect a suppurating adenitis of a moderate degree, and to warn us to be on the look-out for otorrhœa.

Without pursuing this line any further, we may say that, as a result of most careful observations, we have never found a case in which membrane has been present in either nares or larynx in which the diphtheria bacillus has not been demonstrated to have been associated with either streptococci, staphylococci, or both.

2. *Personnel* of the Patient.

In the following table of original statistics compiled from 1000 consecutive cases of diphtheria, the results confirm the deductions of many others, which from time to time have been previously published with regard to **age** and **sex** :—

[Tables.

Table I.

Mortality of Diphtheria according to Age.

Males, ...	533
Females, ...	467
Total, .	1000

Males.				Females.			
Age.	Number of Cases.	Deaths.	Per cent.	Age.	Number of Cases.	Deaths.	Per cent.
Under 1	5	3	60	Under 1	6	2	33
" 2	50	27	54	" 2	21	18	85·7
" 3	55	24	43·6	" 3	30	10	33·3
" 4	74	36	48·6	" 4	43	18	41·8
" 5	70	25	35·7	" 5	48	18	37·5
" 6	65	17	26·1	" 6	43	17	39·5
" 7	40	9	22·5	" 7	44	15	34
" 8	29	6	20·6	" 8	28	3	10·7
" 9	12	2	16·6	" 9	19	9	47·3
" 10	17	2	11·7	" 10	21	3	14·2
" 11	15	6	40	" 11	14	2	14·2
" 12	10	0		" 12	10	0	
" 13	7	0		" 13	9	0	
" 14	11	1	9	" 14	11	1	9
" 15	6	1	16·6	" 15	9	1	11
Over 15*	67	3	4·4	Over 15*	111	4	3·6

* The eldest of these was 43 years old. * The eldest of these was 55 years old.

Synopsis of the above Table.

Males.				Females.			
Age.	Number of Cases.	Deaths.	Per cent.	Age.	Number of Cases.	Deaths.	Per cent.
Under 5	255	115	45·2	Under 5	148	66	44·5
Between 5 and 10	162	36	22·3	Between 5 and 10	155	47	30·3
Between 10 and 15	49	8	16·3	Between 10 and 15	53	4	7·5
Over 15	67	3	4·4	Over 15	111	4	3·6

Synopsis of the whole 1000 *Cases.*

Males and Females.			
Age.	Number of Cases.	Deaths.	Per cent.
Under 5	403	181	45
„ 5 and 10	317	83	26·2
„ 10 and 15	102	12	11·7
Over 15	178	7	3·88

With regard to the death rates in male and female children, the figures in the above table do not agree with those emanating from some other sources.

The most marked difference is that in females, which is 31·7 per cent. in excess of the males in the first two years in our table; whereas it has formerly been observed to be deficient in the ratio of 8 per cent.

Of the cases which occurred between the ages of five and ten years, the Registrar-General's tables, including the figures for twenty years, have given an excess of 30 per cent. On the other hand, there is an increase in the death rate of the males between the ages of ten and fifteen, which is contrary to what we find in the larger tables. It need hardly be pointed out that in tables taken from the returns of Infectious Fever Hospitals the margin of allowance for erroneous diagnosis is far narrower than in the returns of the Registrar-General.

In the 1000 consecutive cases now under consideration, the males are in excess of the females in the ratio of 6 per cent., and this, taken with the extraordinary excess of the females of adult age as compared with the males—the ratio being 3 to 1—clearly indicates the greater exposure of boys of tender years, and is moreover in accordance with the statistics of all respiratory affections.

It has been stated that there is for girlhood, as for womanhood, a greater danger from diphtheria, the difference being one of greater and more sustained exposure to the direct infection. Our

figures, however, do not confirm this statement, and it appears reasonable that, whether in regard to school attendance, association with infected companions at play, or causes of infection external to home, the risk in the case of boys must be greater than that in girls. In adult life it must be remembered how much more likely is the mother, sister, or other female relative and attendant to contract the disease.

The most striking feature in the table is the uniform mortality apparent in the two sexes during the first five years of life. Later, we find a decrease in the female mortality over that in the male sex.

Another interesting point to note is the great proportion of recoveries among the cases, very few though they be, treated in females under one year of age, and the entire absence of mortality in both sexes between the ages of eleven and thirteen years.

Among the cases the youngest was a child of six weeks, and the result was fatal; the eldest male was forty-three, and the eldest female fifty-five years of age, and recovery resulted in both cases. Two females were pregnant during the disease, and both recovered.

These figures are, for the most part, confirmed by Table II., which represents the mortality according to age of all the patients treated in the Asylums' Board Hospitals during 1892 and 1893:—

*** The following Supplementary Table represents the mortality in all the cases treated—11,598 in number—in the Asylums' Board Hospitals during the years 1888-94 inclusive:—

Males.		Females.		Total.		Per Centage.		
						M.	F.	Total.
Admitted.	Died.	Admitted.	Died.	Admitted.	Died.			
5245	1677	6353	1839	11,598	3576	32·0	29·0	30·3

In the year 1894 the mortality in 3666 cases is 28·2 per cent., thus demonstrating a satisfactory though gradual improvement.

Table II.

Mortality, according to Age, in Asylums' Board Hospitals, 1892-93.

Ages.		Males.		Females.		Total.		Per Centage.		
		Admitted.	Died.	Admitted.	Died.	Admitted.	Died.	M.	F.	Total.
Under 1,	1892,	28	14	21	17	49	31			
	1893,	18	15	22	22	40	37			
		46	29	43	39	89	68	63·04	90·69	76·4
1 to 2,	1892,	54	40	54	26	108	66			
	1893,	88	55	78	51	166	106			
		142	95	132	77	274	172	66·9	58·3	62·7
2 to 3,	1892,	77	45	86	45	163	90			
	1893,	117	73	102	58	219	131			
		194	118	188	103	382	221	60·82	56·28	57·8
3 to 4,	1892,	94	48	101	48	195	96			
	1893,	158	90	138	59	296	149			
		252	138	239	107	491	245	54·76	44·76	49·9
4 to 5,	1892,	101	39	139	67	240	106			
	1893,	154	61	185	82	339	143			
		255	100	324	149	579	249	39·2	45·97	43·0
5 to 10,	1892,	301	74	330	89	631	163			
	1893,	403	114	477	119	880	233			
		704	188	807	208	1511	396	26·7	25·72	26·2
10 to 15,	1892,	84	8	125	7	209	15			
	1893,	135	18	163	12	298	30			
		229	26	288	19	507	45	11·85	6·59	8·8
Over 15,	1892,	150	6	264	10	414	16			
	1893,	241	18	369	18	610	36			
		391	24	633	28	1024	52	6·13	4·42	5·0

Grand Total.

Males.		Females.		Total.		Per Centage.		
Admitted.	Died.	Admitted.	Died.	Admitted.	Died.	M.	F.	Total.
2213	718	2654	730	4857	1448	32·44	27·0	29·8

There can be but little doubt that there is an **age disposition** to diphtheria, as well as an **age mortality**, due to two causes, one of which, the disposition to nasal obstruction and enlargement of the tonsils (allusion to which has been already made in discussing the etiology of the disease), and another, the greater tendency in the infant to membranous exudations in all acute inflammatory conditions of the throat, quite irrespective of contagiousness, as compared with the submucous infiltration with œdema in analogous affections when they occur in the adult.

There is also as much hyper-sensitiveness to diphtheria in the young as there is to scarlet fever, measles, and the like, which, moreover, are themselves so frequently the forerunners of an attack of diphtheria. And it is worthy of notice in this connection that, in all epidemics of diphtheria as well as in the large majority of sporadic cases, children are the first to be attacked.

Social status, domestic surroundings, &c.—Although, in its endemic form, diphtheria is rarely manifested in the first instance in houses thoroughly efficient in sanitation, it will, when epidemic, rage equally amongst both rich and poor, the delicate and the robust. But it has appeared to us that when diphtheria attacks members of the upper classes it is often more malignant, and runs a more quickly fatal course than amongst the indigent; the disease finding, as it were, a more receptive soil in the case of those delicately nurtured than in those whose systems are in a manner accustomed to insanitary influences. On the other hand, and for obvious reasons, recovery from the sequelæ when once the acuteness of an attack has passed off is more expeditious and complete in the well-to-do.

Another factor of an untoward prognosis when diphtheria occurs in a family is that the smaller the building and the poorer the service the less likely are precautions against infection to be efficiently pursued. A recommendation of isolation is often interpreted as the herding together of every fresh case in one and the same room, already occupied in many cases by one or more of those previously attacked; some of them may even

have died in this room; and thus the new cases are brought into an already vitiated atmosphere, with the further result of seriously diminishing the amount of cubic air space at command, which in many instances may have been insufficient for even a single case.

Thus we find histories of the pre-existence of mild cases in the same family, or at least cases which have recovered; nevertheless, the prognosis in a second or third case in the same household, however favourable the result may have been in the one first attacked, should—other things being equal—be progressively more carefully guarded in those subsequently infected with the disease.

In the case of an epidemic, the prognostic data of any individual case should be regulated with due regard to the character of the *prevalence* as judged by other cases in the neighbourhood; the source of primary incidence and personal infection must also influence one's forecast, for undoubtedly the virulence of a case may be modified in its intensity by such general and special circumstances.

Clinical character of the membrane.—In the days prior to bacteriology, more importance was ascribed to the appearance of the throat in diphtheria than we should be justified in awarding it in the present day; for while we now know that the exudation may be small in amount, or even—so far as one can see—entirely absent in cases in which, for toxic reasons, a grave prognosis is indicated, it may, on the contrary, be safely asserted that the forecast in respect to the amount of membrane present will be increasingly grave in proportion to the extent of area covered by it, as also in regard to the abundance and the consistence of the exudate. No argument is needed to make it evident that under these circumstances the prognosis is rendered more serious from the two-fold point of view of increased mechanical obstruction to respiration, and the greater opportunity for the generation and absorption of the toxic products of the specific organisms present in the membrane; and it is nothing less than amazing that a contrary opinion should for a moment have been entertained, and should in our present

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knowledge be persisted in. The sinister import of the extent of surface covered by the exudation is further emphasised by a consideration of those cases in which the membrane extended to the lining mucous surface of the buccal cavity, lips and hard palate. Of the former class, there were in our table six examples, of which two died; and of the latter, twelve cases, in eleven of which there was also fatal result.

TABLE III.

ANALYSIS *of* 1000 *cases of Diphtheria, illustrating mortality according to site.*

SITE OF MEMBRANE.	TOTAL NO. OF CASES.	DEATHS.	PERCENTAGE.
Faucial (alone)	666	81	12
Laryngeal (alone)	4	1	25
Nasal (alone)	2	1	50
Faucial and laryngeal	112	51	43·7
Faucial and nasal	165	106	64·2
Faucial, laryngeal, and nasal	49	30	61·2
Membrane involving the buccal cavity and lips.	6	2	33·3
Membrane involving the hard palate.	12	11	91·6

In 5 cases faucial diphtheria was associated with epistaxis.
,, 1 ,, ,, ,, hæmorrhage from the ear.

The above table forcibly emphasises the greater mortality in those cases of diphtheria in which the **nares** are involved, though the figures may come somewhat as a surprise to the majority of medical practitioners who do not yet admit the paramount importance of an open front door to the respiratory passages, and the great influence of obstruction of the same on respiratory diseases in general.

Another evidence of the probable extension of the membrane into the post-nasal space is the fairly frequent occurrence of suppurative catarrh of the middle ear in cases in which the site

of the membrane has been described as faucial, albeit this complieation is not so often witnessed in relation to diphtheria as it is in regard to scarlet fever or measles, even if allowanee be made for the relative frequeney of the different diseases. The aural eomplieation of diphtheria, unlike that of these last-named exanthemata, does not appear to be eharaeterised by a great degree of pain, nor is its prognostie importanee from meningeal inflammation or mastoid suppuration great, although eases of periostitis whieh have required relief by ineisions do from time to time oeeur. It is not out of plaee to mention here that amongst the sequelæ of diphtheria deafness, both in the middle and internal ear, is suffieiently frequent to oeeupy our prognostie eonsideration. It may also here be mentioned that, in one ease of nasal diphtheria, death ensued from meningitis, and no aural eomplieation was to be found. This eireumstanee offers a not improbable explanation of the gravity of nasal diphtheria. For not only do the turbinals eonstitute an extensive and readily absorbent surfaee, but there is a liability to direet eerebral infeetion through the eribriform plate, as has been observed in regard to eerebro-spinal meningitis in whieh the specifie organisms have been found in the anterior meninges.

If we take the whole number of the eases in the foregoing table in whieh the **nares** were noted to be involved, we find that the mortality was as high as 63·4 per eent., whereas the total mortality of the eases in which the **larynx** was implieated was only 49·7 per eent.

In the nasal eases we may fairly inelude six deaths in whieh the exudations have been noted as limited to the fauees. Epistaxis oceurred in five, and hæmorrhage from the ear in one ease; and in all these it is only reasonable to assume that, although membrane was not seen in the anterior nares, it extended to the posterior nasal spaee, and in one case along the Eustaehian tube. No doubt these eases represent a type that is even more frequent.

General Condition.—Having thus eonsidered the features of prognosis in relation to the objeetive evidenees in the throat and

allied regions, a few words must be said as to those general data which may influence our opinion on first seeing a case.

First as to general aspect.—There is really nothing very characteristic in the facial expression of a little patient, if seen on the first or second day, which might indicate to us the grave nature of the malady we are about to combat; and, as will be remarked presently under the respective headings, there is manifestation of early alarm in regard to the ordinary vital functions. If the patient be not, however, seen until after the second or third day of the disease, one will be struck with the peculiar facial cachexia—at once pallid, pasty, and sometimes puffy, though this last feature is held by many to be especially distinctive of scarlet fever.

Diphtheria patients are, as a rule, lethargic, which fact can be particularly noticed in the case of infants, especially as seen in hospital, where they quickly become amenable to treatment; not so much from any change in temperament as from apathy, and this symptom bearing a direct relationship to the systemic poisoning, variation in liveliness, and "taking notice," should be remarked by the physician as one of prognostic value.

Temperature.—One is so accustomed to read and hear of the fever of diphtheria that we almost hesitate to declare our conviction—formed on personal observation and confirmed by others whose experience is much greater—that as regards fever there is little to speak of as compared with the acuteness of the constitutional disturbance characteristic of the disease.

We may refer again to our analysis of 967 cases, out of a total of 1000, in which the temperature was recorded (on an average at the third day of the attack). This shows that in 80 per cent. of the cases the thermometer did not register a higher point than 101° F., while in 30 per cent. it registered a temperature below 99°. Nevertheless, in almost all of these a discount ought to be allowed for what might be termed "ambulance fever," for with hardly an exception the temperatures fell within a few hours of the patient's admission to hospital.

With regard to lowered temperatures, **algidity,** so marked as

to be detected in the axilla, is an occasional late symptom of the disease, and indicative of asthenia. It is one of almost fatal omen. **Rigors** rarely occur in the initial stage with infants, but they may be seen in adult cases. They may also be manifested as an evidence of suppuration in the case of adenitis, or of septic absorption, to be followed by the characteristic chart of pyæmia, or of broncho-pneumonia. Any further remarks would only be to repeat what has already been said on the subject of temperature in the chapter on clinical diagnosis.

Pulse.—The chief distinctive feature of the pulse in diphtheria is its extreme rapidity in proportion to the temperature. The difference is greater than that observed in scarlet fever, for in the latter disease the temperature continues for a much longer period at a higher degree above the normal, whereas in diphtheria its tendency after the first day or two is sub-normal. The pulse-rate as well as its force is greatly influenced not by pyrexia, but by the asthenia, which is the uniform and far-reaching result of the toxic poison. A rapid pulse which does not vary much in rate for days is not of altogether unfavourable significance, provided that it remains regular, and that the gradual return to the normal be not unduly prolonged. But if the acceleration is progressive and is coupled with irregularity in the rhythm and force, the prognosis becomes proportionately grave. It will, therefore, be understood that sub-normal temperatures coupled with a rapid pulse-rate are not, taken by themselves, of much prognostic value. "An extremely rapid and feeble pulse is of grave import; a very infrequent pulse is of fatal significance" (Jenner).

Adenitis. — The subject of glandular inflammation and its diagnostic significance were also treated fully in Chapter VII. Of the 283 deaths which occurred in our 1000 cases, suppurating adenitis was present in 32 instances, or in other words in 11·3 per cent. of the fatal results. Happily, this complication hardly demands very serious consideration as an element of vital prognosis. Nevertheless, when suppuration has taken place, the results as regards life may be influenced by its early recognition

and surgical treatment: for while on the one hand a discharge may possibly have a certain beneficial effect on the poisoned system, the concurrent cachexia cannot fail to retard convalescence, and even to increase the gravity of other data of evil omen. There is, of course, always a danger of general septicaemia by direct metastasis. This is sometimes evidenced by the pains which occur in the joints in such cases.

The following case well illustrates the sequence of clinical events in connection with this complication, especially with regard to temperature:—

V. W., a female aged 4 years, first seen on September 18th, on the third day of the disease.

On admission.—The throat was inflamed, and thick membrane was present on the right tonsil. *Temperature*, 99° F. No albumen. *September 22nd.* Membrane was seen on the left tonsil, that on the right having nearly disappeared. *Temperature* was 98·4°. Urine contained a haze of albumen. *October 6th.* The left side of the neck very swollen, red and tender to the touch. *Temperature*, 100°. *October 11th.* Fluctuation detected over the site of the swelling; on the following day an incision made into it, and 4½ ounces of characteristic pus evacuated. The cavity irrigated with warm boracic lotion, and a drainage tube inserted. *Temperature*, 99°. Doing well; discharge from the wound has decreased. Strabismus noticed. *November 3rd.* Drainage tube removed, the discharge having practically ceased. Palatal paralysis. The little patient made a good recovery.

3.—Complication of the Vital Functions.

Cardiac.—It is extremely difficult to determine, even after careful autopsy, what is the proportion of cases in which cardiac failure is the sole responsible cause of death. In our table of 1000 cases, 18 were noted out of a total of 283 deaths as due to heart failure. But these figures under-estimate the cause of death from this source, and we believe that, in a large number of cases where the patient dies of asthenia, *heart failure* would in almost every instance represent the exact mode of termination, although it is more common for them to be certified as dying of *apnœa*, albeit there is no evidence of obstruction of the air passages, or disease of

the lungs. A fatal issue due to this cause may be brought about in several ways, of which the following may be mentioned:—(1) Direct effect of the toxic poison on the system; (2) Clots in the ventricles or in the great vessels of the heart; (3) Cardio-pulmonary paralysis; (4) Vomiting and other causes acting through the vagus; (5) Ulcerative Endocarditis, Myocarditis and fatty degeneration of the cardiac muscle.

Respiratory.—The lungs are very liable to be involved in diphtheria as an extension of the inflammatory processes from the upper air-passages, and we may mention the following as being the most generally recognised pulmonary complications:—Acute in-sufflation, collapse of the lungs, broncho or lobular pneumonia, croupous or lobar pneumonia, pulmonary apoplexy, capillary bronchitis, and lastly, septic pneumonia. Implication of the air-passages may result in extension of the exudation to the bronchi, and even to the smallest tubes, in which cases it will be found to have lost its membranous quality, and is almost of fluid consist-ence though still somewhat adherent; but probably the most frequent pulmonary complication is broncho-pneumonia.

Paralysis of the muscles of the larynx may lead to collapse of the lungs, acute insufflation, and congestion. Moreover, in cases of paralysis of the upper sphincter of the glottis, or of the palate or pharynx, the entry of particles of food and other foreign matter into the air-passages is liable to set up acute broncho-pneumonia. Portions of sloughing tissue, pus, &c., de-rived from the upper respiratory organs, may also be the cause of a septic form of inflammation of the lungs, which last may also occur as a result of the acute bacillary toxæmia. Obstruction in the nares is also a factor in the production of pulmonary congestion and of pneumonia which should not be overlooked.

In our systematic treatise we have recorded the case of a child in whom a peculiarity of respiration resembling "Cheyne-Stokes" breathing, or rather that of Biot, was observed on three nights during the acute stage of diphtheria while the patient was asleep. This symptom was only apparent when the nasal cavities were

blocked, and was relieved by treatment directed to a re-establishment of the normal nasal breathing.

Renal.—*Albumen*, at any rate in hazes and traces, is to be found in the urine in fully one-half of the cases of true diphtheria; but it has been shown not to possess much diagnostic value, because it is also present in many other cases of affection of the throat of a more simple nature. Equally, its presence cannot be said to be of great prognostic importance, if only transitory, as we are in the habit of considering it in all cases in which albumen does not persist for longer than three days; nor is its presence to be much regarded *so long as the amount of urine excreted is not diminished in a marked degree*, nor unless albumen be present to the extent of more than one-eighth, in which case it is almost certain that there will be at least partial suppression. If, in addition, the urine contains epithelial cells or casts, or if hæmaturia ensue (a rare occurrence), the outlook is rendered all the more grave.

Death from *convulsions* and *coma*, rare as it however is, may as a rule be safely asserted to be the result of *uræmic poisoning*, though the possibility of a cerebral explanation must not be lost sight of. A peculiarity of the uræmia of diphtheria is the clearness of intelligence up to the moribund stage, or even up to cessation of life itself. Green vomiting and green diarrhœa may be taken as premonitory of anuria, especially in that form due to vaso-motor causes.

The mortality due to *nephritis* and its results according to our tables was 2·7 per cent., and more detailed examination would appear to show that there is some relation between this renal complication and nasal obstruction, which will readily be understood by those who recognise the influence of the last-named condition on the oxygenation of the blood. Moreover, the same trouble appears to indicate that the frequency with which suppression of urine is associated with epistaxis is more than accidental.

A possible explanation for the frequency of nephritis may be found in the fact that a considerable proportion of cases of

diphtheria follow on scarlet fever, in which, however, as a rule albuminuria occurs at a later date than in diphtheria; though in both diseases it often continues long, and may be responsible for permanent renal mischief.

Laryngeal. — A laryngoscopic examination should always be made whenever possible, and we have over and over again used it in the case of very young children. Its difficulties usually occur to those who seldom employ the mirror, rather than to those who have acquired aptitude and dexterity by daily practice.

In infants and children up to the age of ten years, auscultation is apt to be unsatisfactory in cases of laryngeal obstruction; so that we have rather to be guided by the coarser indications of the thoracic movements, such as retraction of the ribs and abdomen, and clavicular upheaving, and the noxious effects on the general circulation, such as increasing cyanosis.

It must be admitted that the prognosis in respect of laryngeal obstruction can be influenced by the powers of observation in the practitioner and his promptitude to adopt suitable surgical measures on early monition of their necessity.

Moreover, we must not allow our forecast to be too much guided by the presence of *cough*, which, when partaking of the character variously called *laryngeal, metallic, brassy,* and *croupy*, by no means necessarily depends on the presence of membrane, but may be due to inflammation without exudation, to implication of the laryngeal nerves, superior or inferior, causing respectively spasm of the tensors, adductors, or abductors of the larynx, in each of which case the vital dangers will be of diverse degree.

Indeed, with regard to *laryngeal stridor*, so frequently witnessed in diphtheria, it is a question worthy of consideration whether it may not be more commonly of nervous origin than is generally supposed. Our own experience leads us to suggest that such an association would be confirmed in a large proportion of cases were laryngoscopic examinations in cases of diphtheria made more frequently than they are at the present time.

Dr. Gee, on the subject of cough, has touched on this point, acutely remarking on the probability "that when patients suffering from diphtheritie paralysis die, suffocated from inability to expectorate, and the lungs, *post-mortem*, are found to be collapsed, the inability to expectorate is by no means always due to paralysis of the inspiratory or expiratory muscles. On the contrary, those muscles may act well and yet the patient be unable to cough and expectorate adequately." Dr. Gee thinks that, "in these eases, the difficulty lies in the muscles of the glottis. The voice is often very weak; the cough is very ineffeetual;" and he supposes "that the patient is compelled to eough with a glottis more or less open, and is thus brought to a eondition similar to that of a patient upon whom traeheotomy has been performed. Aeeumuation of the bronehial secretions, imperfeet expansion, collapse and eongestion of the lungs, follow; henee suffoeation and death."

The prognosis with regard to surgical proeedures which may beeome neeessary during the eourse of an attack of diphtheria will be more appropriately eonsidered when the subjeet of surgical therapeusis is diseussed.

No further allusion need here be made to the relative prognostie value of a faueial, a nasal, or a post-nasal site of the exudation, but it may be noted that, though rarely, membrane does sometimes extend to the **œsophagus,** to the **stomach,** and even the **intestines,** in whieh the lesion is found to arise in Peyer's patehes—the *intestinal tonsils,* in faet.

A case of diphtheric enteritis came under my observation in the year 1884. The patient, a general practitioner, was attacked with all the symptoms of intestinal obstruction whilst actively engaged in attending a large number of cases of epidemic diphtheria; marked asthenia was exhibited early in the disease, and the illness terminated in death from perforation and fæcal escape into the peritoneal cavity. At the *post-mortem* examination several diphtheritic patches and ulcers were found in the small and large intestines. The real nature of the case was quite unsuspected till the autopsy revealed it.

During the epidemic of diphtheria at Ealing in 1887, two cases came under my notice of sisters who, with others, were attacked in a school.

One had, in common with other pupils, pharyngo-laryngeal diphtheria, from which she recovered; the other had no throat symptoms, but died of perforative peritonitis—the result, as we believed, of diphtheric enteritis. Concurrence with this opinion was expressed by Dr. Wilson Fox, who saw the case, but no necropsy was made.

Not a few cases have been reported of diphtheria of the **anus** and **female** genitals.

Hill has recorded two primary cases of diphtheria of the perineal region which occurred in a father and daughter. The disease was supposed to be contracted through using an insanitary water-closet. The father, aged 40, had false membrane on an old eczematous patch near the anus, which was followed by typical paralysis. There was no false membrane in the throat. The daughter, aged 9, had some weeks afterwards primary diphtheria on the vulva, which spread to the vagina, and perforated the recto-vaginal wall. In this last case there was also false membrane on the throat, which extended to the lungs, causing death.

All these varieties are, so far as the records go, of very fatal character.

Neuroses.—In the 2848 cases of diphtheria treated at the various Metropolitan Asylums' Board Hospitals in 1893, paralyses were noted in just 14 per cent., and this proportion agrees in the main with that deduced from our own table of 1000.

These figures will probably be received with surprise by those who have been accustomed to judge of the truly diphtherial nature of an attack by the occurrence of paralytic sequelæ, and common experience would certainly have prepared many of us to accept such a percentage rather as representing a high estimate of the absence of paralyses, than as an ordinary one of their presence. In respect, however, of these symptoms there is a great variation which is regulated by the type of an epidemic.

Neuroses due to diphtheria have to be considered from the prognostic points of view :—

(1.) As they may occur in the acute stage.

(2.) During convalescence.

(3.) As late manifestations, by which is meant at an interval of more than four weeks after the commencement of the attack.

The neuroses are due to a toxic, segmentary neuritis, which leads to interruption of the nerve supply of the muscles affected; and consequently to fatty degeneration of the respectively innervated muscles. The prognostic value of any neurosis depends not only on the stage of the disease at which it occurs, but more particularly on the physiological and functional importance of the muscles involved. During the **acute stage** we must be on the watch for neuroses involving the **cardiac** and **respiratory** nerves, on which depend cardiac syncope, paralysis of the diaphragm, and pulmonary collapse.

The most usual order of appearance of the paralyses of convalescence is—First, those affecting the palate, evidence of which is manifested by a **nasal tone** in the voice. This is caused by a dropping of the soft palate, with escape of air through the nose at every consonantal sound, instead of only with those normally nasal, namely, "M" and "N." **Anæsthesia** of the palate is associated with this form of paralysis. In infants, where palatal paralysis is emphasised, starvation may occur through inability to suckle, a circumstance which (as Morell Mackenzie pointed out) constitutes one of the greatest dangers in those cases where the diphtheric exudation involves the nares.

(2.) Next in order, paralysis of the muscles surrounding the **laryngeal vestibule**, otherwise the superior sphincter of the glottis, is observed, which leads to the passage of fluids into the glottis, and to nasal regurgitation. Paralysis of the **constrictors** of the **pharynx** follows, and more rarely that of the involuntary muscular fibres of the **œsophagus**.

(3.) **Ocular** paralyses are next in order, and we may have ciliary paralysis, most frequently bilateral, producing difficulties of accommodation; or by implication of the sixth nerve, paralysis of the external recti muscles, producing a converging strabismus, which is about the only variety of axis deviation met with in relation to diphtheria.

Slight **facial paralysis** has also been occasionally noted. One case occurred in our series.

The **trunk** and **limbs** may be, and frequently are affected; the neuroses being both **motor** and **sensory**. The latter are indicated by numbness, creeping and formication, hyperaesthesia and intense neuralgia. These sensory manifestations, however, are of a somewhat later epoch than the motor paralyses, which affect prehension and locomotion.

Paralysis may also involve the **visceral** muscles, and when attacking the **diaphragm**, the **intercostals**, or the **heart**, are of most serious import in regard to the vital prognosis, and may be responsible for sudden or rapid death, sometimes at so long an interval after the first appearance of the disease as to have been altogether disregarded as a probable event.

The **bladder** may be involved, but in cases of anuria which recover, the atony of the vesical muscles may also be due to spasmodic contraction of the walls of a bladder which has remained empty for an unduly prolonged period.

The muscles of the **lower bowel** and **rectum** may also share in the paralytic affection; constipation is, of course, the result, but as a rule the sphincter muscles are not involved.

In some of the worst cases the paralysis involves nearly all the muscles in the body.

Lastly may be named **reflex** paralyses, as exemplified by the early loss of knee jerk; this is sometimes preceded by exaggeration. In many cases normal reflex only returns after an interval of several months.

Hughlings Jackson has drawn attention to the fact that loss of reflex is one of the very earliest prognostic symptoms of nerve impairment in cases of diphtheria, and the following is of interest in this connection:—

A young Jewess, aged 17, was admitted into the North-Western Fever Hospital from a general hospital on the notification of the house-physician who had gained his experience of diphtheria as an assistant medical officer under the Asylums' Board. The patient applied complaining of sore throat, for which she had been already treated at home. On examination there was only to be seen some faucitis with a scrap of membrane on one pillar not larger than a pin's head; there was, however, entire

absence of knee-jerk, and it was on this ground that notification was made.

No other symptoms presented themselves during the patient's stay in hospital; temperature, pulse, appetite, throat condition, and general health remaining normal. Nevertheless, after the ordinary interval, well-marked palatal and other paralyses of severe type were manifested.

An attentive consideration of the many diverse data already given is necessary in order that the clinician may be able to rightly interpret many other portents which have not been individually named, such as pain in the throat, ear, head, trunk, and limbs, anorexia, dysphagia, insomnia, and delirium.

Date and mode of death.—It will doubtless have been noted that no prognosis as to the date of death has been given, the reason for which omission is due to the circumstance that in this element there is an equal uncertainty and as much variability as in any of the other data offered for our consideration.

Sudden death may occur from suffocation, asthenia, cardiac, renal, pulmonary, paralytic, and other causes. In the first week a fatal termination may ensue from obstruction to respiration and its consequences, either with or without operative interference, when the larynx is involved. Paralysis of the respiratory or cardiac functions may be responsible for a fatal termination at a quite early or at a later date; again, the formation of a fibrinous clot in the heart or great vessels, may lead to a sudden and unexpected end.

Renal complications, albeit that they are manifested as early as the third day of the disease, may not result in death for two or even three weeks. Moreover, some of these complications, as well as others previously alluded to, may cause life to be held in the balance for a long period, and it is, therefore, not too much to say that no patient should be declared "out of the wood" within a period of at least six weeks from the initial symptoms of the attack.

Finally, the prognosis of diphtheria may be qualified when it occurs as a sequel of a previous illness, the forecast being *cæteris paribus* more serious when following an attack of scarlatina or

other specific fever, or of epidemic influenza. On the other hand, any independent and comparatively mild malady which may supervene on an attack of diphtheria during the period of convalescence, will assume unduly grave proportions in consequence of the neurasthenic condition of the patient in whom it is manifested.

CHAPTER X.

THE TREATMENT OF DIPHTHERIA AND ITS ASSOCIATES.

GENERAL—LOCAL—OPERATIVE.

NEITHER the discovery in 1884 of the specific micro-organism of diphtheria nor of its toxic products, which five years later were shown to account for the systemic poisoning, have tended to arrest the variety or the multiplicity of the constitutional and local remedies recommended for the cure of the disease, nor to prevent its treatment being dictated on any other than an empirical and often unscientific foundation; for during the last quarter of a century hardly a week has passed without "bold advertisement" of a new specific for diphtheria, either constitutional or topical.

Considering the disease in its aspects of danger to life, which are synchronous with the different stages of its progress, let us discuss the various means at our command to combat the respective eventualities.

1. **Primary hygiene.**—Faults in hygiene being in our opinion largely responsible as predisponents to specific infection and as greatly aggravating the nature of an attack, we should first take care that the patient is placed in a light, well ventilated chamber, with ample air space, but without draughts, and with as few as possible hangings and articles of furniture likely to retain the contagium.

First, the child must be isolated as far as possible from other inmates of the house: the temperature of the room should be regulated according to the season of the year, and the barometric

condition of the atmosphere. If the case occur in the winter months, the wind being in the north or north-east, the air of the room is not only to be well warmed, but also softened by steam, impregnated with eucalyptol or some other fragrant essential oil; if in foggy weather, with wind in the south-east, a drier warmth is indicated. If, on the other hand, the case occur during the summer, fresh air, with precautions against draught, may be admitted to a much freer extent, and steam may be almost dispensed with.

If more than one patient be placed in one room, there should be at least 2000 cubic feet of air space for each, with a further liberal margin for nurse and friends.

The room should be maintained, even in the coldest weather, at a temperature not exceeding 65° F., nor should it be overcharged with moisture, except in cases of laryngeal diphtheria, the suitable atmospheric conditions for which will be later described.

The patient should be kept perfectly quiet as regards bodily movement, and should be nourished by means of "feeders," so as not to allow even the raising of the head from the pillow, and he should not be allowed to rise from this recumbent position for any reason whatever.

Endeavours to rouse children to notice picture books or to play with toys is to be avoided until at least the tenth or twelfth day, when reasonable fear of cardio-respiratory failure may as a rule be held to have passed away.

General Treatment.

As an adherent to the view that micro-organisms are not the only factors in the contagious processes of diphtheria, but that we have also to deal with a chemical virus, for the most part of an albuminoid constitution, our treatment has been laid down on the following lines:—

By **internal remedies** to aid the system in the elimination of the chemical virus by the ordinary *excretory channels*—skin, bowels,

kidneys, lungs, &c. This procedure may be more active and prolonged in non-bacillary diphtheria, in which there is less fear of increasing prostration.

Recognising the prostrating character of the toxic products of diphtheria, and the infectious tendency of its associated organisms, to administer remedies calculated to reinforce the debilitated vaso-motor system and to improve the quality of the blood.

To combat the poisonous effects of the virus on the system by treating cardiac depression, renal inadequacy, and other constitutional symptoms as they arise.

To sustain the vital powers by a **diet** at once nutrient and easily digested, and by the administration of **alcohol** on definite indications, and at regular intervals.

By **topical measures** to render the membrane more easy of separation, and to annihilate micro-organisms.

To adopt such **operative treatment** as will remove all mechanical obstacles to respiration.

Proceeding to details—in all cases of sore throat, even before the diphtherial nature is determined, it is well to begin with a purge; and in the case of children, even if diarrhœa be present. For this purpose a small quantity of calomel or grey powder is the best, and this should be coupled with antimony in the form of James's powder for its antipyretic and diaphoretic properties.

At the same stage, there still being no evidence of membrane, but simply local inflammation, we should then prescribe a mixture [Formula 1] containing remedies in combination with a threefold intention—namely, by means of salicylate of soda to reduce general pyrexia, and local inflammation; to this we add chlorate of sodium, for possibly oxidising and blood improving properties; and lastly, these are administered in a medium of decoction of cinchona, which has not only a certain germicidal action, but constitutes a valuable tonic, coupled with more astringent properties than are obtained in its alkaloidal form as quinine.

The soda salts are always to be preferred to those of potash in this and all diseases manifesting symptoms of depression; the salicylate is to be given in very moderate doses, and would be better omitted should there be any symptom of cardiac complication.

The moment we see membrane, and recognise its diphtherial character, we should administer iron, and give it freely and fully, preferably in combination with potassium or sodium chlorate [Formula 2].

One may be excused for saying in passing that it cannot but be gratifying to the clinician that all the advancement in scientific knowledge of the etiology of the disease, which we have so gratefully recorded, has but confirmed the wisdom of the internal treatment pursued in this country for the last forty years, albeit it has been prescribed on what the new school might consider unscientific and empirical grounds. Iron and chlorate of potash or soda still represent the sheet anchor of our constitutional treatment of diphtheria.

Having made trial of the salts of mercury, especially the biniodide, in diphtheria, we have been forced to the belief that they do not form inert chemical compounds with the toxic products of the diphtheria bacillus, and we are quite in agreement with those who say that a diphtheria patient has already absorbed in his system sufficient poison from the organisms of the disease, to make us hesitate in prescribing drugs which can in no way give him strength to fight against so prostrating a malady, and without any great stretch of fancy may but add to his embarrassment. It may be said, however, that mercuric biniodide is of the highest value in many forms of *pseudo-diphtheria* of coccal origin and septic characteristics [Formula 2]. It is to this class that the remedy should in future be limited; remembering, in addition, that it constitutes a prophylactic of tested utility, taken internally in small doses, or used highly diluted as a gargle by those exposed to infection.

So far as drugs are concerned, cardiac depression is to be combated by the addition of strychnine to the iron mixture

[Formula 4], or by the hypodermic injection of the drug. The amount of strychnine which may be administered in this manner even to children of quite tender years without harm, is nothing less than astonishing. As much as 5 minims of the P. B. solution will produce none but good effects when given subcutaneously, even as often as three or four times in the twenty-four hours.

Strophanthus and cactina are also cardiac tonics which have been found useful in these cases.

As to other constitutional symptoms:—Respiratory troubles other than those depending on the presence of membrane in the air passages are due to two causes, cardiac (vaso-motor) and septic, and the remedies have already been discussed which are suitable for each of these conditions. Expectorants of a depressing character should be avoided. Anorexia, vomiting, diarrhœa, and constipation, are all, so far as remedies are concerned, to be regarded as signs of diphtherial asthenia or of coccal sepsis.

On the first sign (and in some instances before it occurs) of diminution in the quantity of urine excreted, a mixture of acetate of ammonia and perchloride of iron [Formula 5] is of the greatest service, both as a tonic and diuretic. In the practice of some of the medical superintendents of the Asylums' Board Hospitals, this mixture is given as a routine treatment, and in the case of infants, the perchloride of iron may be exhibited in the form of a drink, made palatable by the addition of syrup or saccharin, at frequent intervals, in fact, as a thirst-quencher [Formula 7].

It has to be remembered that anuria may be due to two causes; one to parenchymatous inflammation of the kidney, probably of streptococcal origin, and the other to vaso-motor inhibition, the direct result of the diphtherial toxæmia, and each will require to be treated on its special indications.

Our own experience is, that when it is due to the first cause no remedy is of avail, but nevertheless vapour baths, wet packs, and the like should be tried. Neither jaborandi nor pilocarpine have been found of service, and, indeed, are rather contra-indicated on

account of their depressant effects. When the anuria is of vaso-motor origin it may be of only transitory occurrence, liable to relapses and remissions, and, in happy exceptions, finally conquered. The remedies indicated are naturally of the nature of nervine stimulants. When the suppression is due to asthenia the measures just mentioned must be moderated, so as to guard against further depression, and stimulants and analeptics may require to be given in increased doses.

Diet.—For the first few days all food should be of a fluid character, consisting for the most part of milk, beef-tea, and broth, which in some instances may require to be peptonised. Thirst is not a characteristic in diphtheria, except in cases of suppression, and in these circumstances the iron drink, previously mentioned, is to be freely administered, and in other cases barley water with chlorate of potash. Oranges and lemon drinks are both grateful, and, on therapeutic indications, useful.

Ice, being very grateful, may be given to children in the form of frozen milk or frozen beef-tea. Theoretically a diabetic diet may be said to be indicated in all microbic diseases; it is therefore worthy of consideration whether saccharin should not be temporarily substituted for sugar for all purposes of sweetening during the illness.

So soon as membrane has cleared, fish, vegetables, and rice pudding may be added, and as early as possible full diet should be prescribed, preference being of course given to mutton and poultry.

Mutatis mutandis, the same rules for diet should hold good with adults as with children.

Alcohol.—It would be difficult to point to any children's disease in which the benefit of alcohol is more markedly illustrated than in diphtheria, but in view of later eventualities in the course of an attack which would call for renewed and increased stimulation, it is well to commence with small quantities, so as to hold so valuable an ally to some extent in reserve.

So soon as the temperature falls to sub-normal, and whenever the

pulse gives indication of cardiac enfeeblement, alcohol—preferably in the form of brandy—should be promptly and liberally given in regular doses, both as to time and quantity, the latter to be increased in the event of a tendency to syncope or collapse. Experience proves that brandy may be administered in comparatively large doses to very young patients in this disease. A teaspoonful every hour to children under five years of age, and double that amount up to ten years will be well borne. Alcohol is *a priori* contra-indicated in excessive albuminuria, parenchymatous nephritis, and anuria.

A word or two may be said here in regard to the treatment of paralytic *sequelæ.* For these conditions the phosphates of iron, quinine and strychnia should be administered perseveringly, and preferably in the form of Easton's syrup. So soon as there is reduction of inflammation, electricity, either in the induced or constant form, as indicated by the reactions, is to be employed. Strychnia has been advantageously employed by us hypodermically, not only in the acute stages, as already mentioned, but in restoring lost muscular power in those cases that do not yield to electric stimulation.

2. **Topical remedies** in diphtheria have to be considered with a view of preventing extension of membrane and of favouring its separation, (*a*) because of its liability to cause death by mechanical obstruction to respiration; and (*b*) from the circumstance that the local exudation constitutes the "brewery," as it were, of the bacillary products—the toxines—which are responsible for the systemic poisoning. This class of local treatment may be called *internal,* while *external* topical measures are those which are capable of affording relief of the external glandular inflammations.

The first points in local treatment to which our efforts will be directed, namely—the prevention of extension of membrane, promotion of its separation, the destruction of the bacilli, and, lastly, the prevention of toxic absorption are so intimately associated that they may be conveniently considered together. It will, however, be necessary to make certain distinctions, not so much

in the constituents of the remedies as in the media in which they are exhibited, and in the method of the topical application according to the site of manifestation. In the first place, we shall consider that class of cases in which the whole local area of the disease is exhibited on oral inspection; this includes those cases in which the site of the membrane is the **tonsils, fauces, palate, and the buccal cavity.**

Foremost among local remedies come **solvents** of the membrane. To this form of treatment we have given much attention, and we have made repeated experiments with some of the different fluids which have from time to time been recommended.

As a result we have found that, though no chemical agent possesses the property of effecting any actual solution of the membrane, an alteration in its character does appear to ensue. Membrane macerated in pure *lactic acid*, undiluted, became soft, translucent, and jelly-like. Pieces of exudation from the same subject similarly treated in *lime-water* were rendered more friable, but no thinner; and this molecular change was more perceptible with *saccharated lime-water*. The solutions were raised to boiling-heat, and lowered to freezing-point; but the experiments were not affected by the temperature of the fluid employed. Taking into consideration the fact that one cannot apply such solutions quite undiluted in the throat—that one cannot exclude air, even with all the balsamic application in the world, especially when laid over a moist surface—that one cannot obtain a direct temperature influence either with steam inhalation or by sucking ice to anything like the degree that was obtained in these experiments, we have come to the conclusion, fully borne out by clinical experience, that these fluids possess no solvent properties whatever, but that lactic acid, not diluted to the high extent hitherto in use, but applied pure—or rather of pharmacopœial strength—[Formula 9] by the surgeon at least once or twice a day, and only moderately diluted—say 1 to 4—every three or four hours by the nurse [Formula 10], has some considerable influence in loosening the molecular cohesion of its particles in a manner more favour-

able to separation than lime solutions, which appear to us quite valueless. Doubtless the efficiency of lactic acid is due in a measure to the fact that an acid medium is inimical to the bacillus. *Perchloride of iron* [Formula 11] has long enjoyed a high repute as a local application, notwithstanding it has not the slightest influence on the disintegration of the membrane. Its taste, and a certain amount of discomfort occasioned by coagulation of the albumen of the oral secretions, constitute an objection to its use not readily to be overcome in practice.

Carbolic acid has no solvent action on diphtheric membrane when employed experimentally on removed portions. As a germicide, both carbolic acid and carbolates occupy a much lower position in the scale than was formerly ascribed to them. *Sulphur*, whether as insufflation or as *sulphurous* acid or as *sulphites*, has given good results, and its use is justified for the twofold reason that it is an efficient germicide, and that it acts both systemically and locally. *Papaine* and *resorcine* are said to act very efficiently as solvents; but experiments that we have made have led us to think that their digestive and solvent action is too feeble to be of practical value. We are quite in accord with those who consider that *caustics* are harmful, chiefly because of their liability to injure contiguous healthy tissue, and thus offer a fertile soil for extension of membrane. On this same ground we cannot agree with Blöebaum of Coblentz, who has reported successful results from galvano-caustic applications, made in the belief that they destroy the micro-organisms of the disease. We agree also with those who think that mere *astringents* are useless. Alkaline solutions, as of *bicarbonate of potash* or *soda*, are advocated by Schech as solvents. As such they have no power, nor can they exercise any remedial action either on the bacilli or their toxic products. *Boric acid*, although but of feeble germicidal powers, is agreeable, being not only non-irritant, but in a measure healing. It is therefore of more usefulness after membrane has separated than before [Formula 20]. *Peroxide of hydrogen* has been highly vaunted as a topical remedy in diphtheria, and theoretically

should be almost ideal. Unfortunately it is too unstable to be of practical utility.

Truth to say, we have been so well satisfied with *lactic acid* that we have been loth to try any other local remedy. We have not found it injurious to contiguous healthy tissues—that is to say, wherever the epithelial layer is entire. Its action appears to be limited almost solely to unhealthy tissue, promoting its disintegration by a process analogous to that of digestion; there is, it is true, some circumferential inflammation, but as this is only of the degree of healthy reaction and leads to the outpouring of scavenging leucocytes, it is to be regarded as a desirable result.

Coming to the best method of removing the membrane, or at least of applying the solution, it has been generally taught that tearing away, or scraping off the exudation is as useless and injurious a proceeding as would be similar treatment of the pustules of smallpox, and is even dangerous, for the reason that it leads to more thorough systemic intoxication; but a diphtheric patch is probably more comparable to a chancre of syphilis than to an exanthematous rash. We have always practised some degree of friction of the diseased surface with a soft but firm applicator well charged with the lactic acid solution, and we have been better satisfied with the results when more or less the membrane has been detached. For this purpose, in the case of children, we employ a swab formed of the index finger well swathed with lint and soaked in the solution; instructing the nurse to use, both for children and for adults, an aluminium, whalebone, or vulcanite rod with a firm head of absorbent wool.

Watson Cheyne, who, like ourselves, considers diphtheria as "from first to last a local disease, the general symptoms being merely due to chemical poisoning," advises "stripping off the false membrane with forceps, &c., as far as possible, and then applying a watery solution of bichloride of mercury, so strong as 1 in 500." He also urges frequent gargling with a weaker solution, 1 in 2000—all this being combined with carbolic acid sprays.

Personally, we believe the time will soon come when removal of

the membrane by surgical procedure will be generally acknowledged to be as efficient as it is scientific.

The means of removal, whether sponge, probang, forceps, or vulsellum, is unimportant so long as removal is thoroughly performed. If, after detachment of membrane, a mercurial application be preferred to that of lactic acid, which we place first on our list, the **biniodide,** as a non-precipitator of serum-albumen, would appear to possess advantages over the bichloride. It can be used in the form of either spray, pigment, or douche with a syringe, and in a strength of 1 in 2000 to 5000. The results of syringing the throat with a solution of bichloride or biniodide of mercury are certainly excellent [Formulæ 16 and 17].

Two or three therapeutical hints in the employment of mouth washes may here be given:—1. That all applications to a diphtheric throat should be of as high a temperature as can be borne, as thereby their microbicidal activity is increased. 2. That both alcohol and glycerine so often prescribed in combination with antiseptic throat washes are said to interfere with the germ-destroying properties of both mercury and carbolic acid. Lastly, it is probable, in view of the readily soluble character of the toxines of diphtheria, that the mere irrigation with water is of direct value, and this may be accepted as an argument for not unduly fortifying this valuable form of remedy with adjuvants capable by their own toxic properties of introducing other noxious elements.

The instrument—specially designed by us for this form of treatment—is here illustrated (Fig. 57), and consists of a more or less curved metal tube, the end of which is pierced with several holes, and attached to a large rubber ball. This instrument can be introduced behind the teeth into the mouth, or back into the post-nasal space, when it is desirable to reach the pharyngeal vault.

The irrigation and cleansing of the throat may be varied or alternated with the use of a chlorine wash [Formula 18], especially in cases where the membrane is slow to clear away.

The recent experience of Loeffler is interesting as confirming, by scientific means, the teachings of a sound and long established empiricism, and is well worthy of quotation:—He found that the bacillus of diphtheria may be killed in twenty seconds by perchloride of mercury, chlorine water, carbolic acid, or a solution containing turpentine and carbolic acid. But it not being always practicable to keep these topical applications in contact with the diphtherial membranes for so long a time, he endeavoured to discover other substances capable of more quickly destroying the bacillus. In the course of his researches he found that sesquichloride of iron, dissolved in equal parts of water, or in the proportion of 1 to 2, as well as other preparations of iron, kills the bacillus with twice the rapidity. Having also noticed that certain

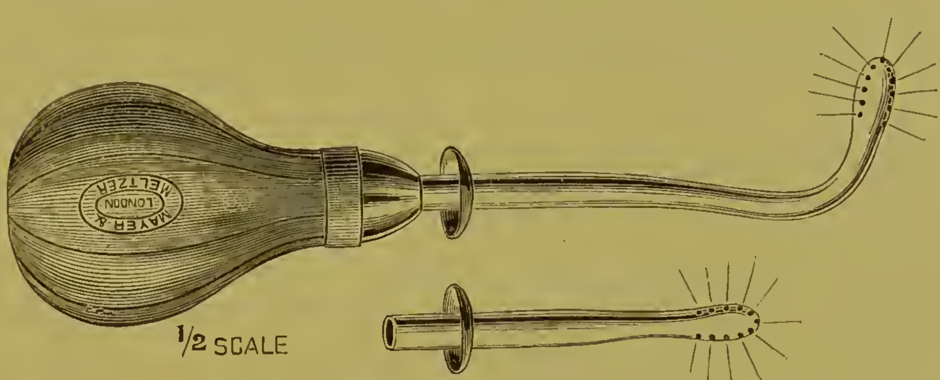

FIG. 57.—Syringe for irrigation of mouth, fauces, and post-nasal space.

essences, such as benzol and toluol, interfere with the development of the bacillus of diphtheria, he investigated their action on animals, and afterwards on man. For the latter purpose he employed a mixture containing iron, toluol, and creolin or meta-cresol. Finding, however, that this solution produced a marked smarting sensation in the throats of children, he added to it menthol [Formula 21].

A cotton tampon steeped in this solution is applied to the affected parts twice in succession for 10 seconds, and this treatment is repeated every 3 hours, until all the local symptoms have disappeared, which ordinarily occurs within 4 to 5 days. While the affection is still local, it may be arrested in its course by this

solution; bacteriological examination will show that all the bacilli in the membranes are killed. Loeffler reports that in 96 cases treated in this manner, three-fourths of which were shown by bacteriological examination to be true diphtheria, not a single death occurred.

We have given this solution a fair trial, and have come to the conclusion that it is more useful in pseudo-diphtherial than in the true bacillary forms of membranous throat inflammations. Probably the excess of alcohol contained renders the remedy, as prescribed by Loeffler, less active, but we have not presumed to change it.

Gargles we do not largely advocate, first, because they are seldom efficiently used, except by the method of Von Troeltsch, which should never be employed when the ingredients are of such a nature as to be capable of doing harm, if inadvertently swallowed; secondly, because the act of gargling necessarily entails the patient's rising from the recumbent posture in bed; it, therefore, should only be exceptionally ordered in cases where the disease is of a mild character, and even then only for patients who have passed the age of puberty. Lastly, it throws the muscles of the throat into irregular activity, and may therefore in a measure favour palatal and faucial pareses.

As a **summary** of the foregoing observations, we would counsel the application of lactic acid to the diseased surfaces, with such a degree of firmness as is sufficient to detach the membrane at its edges, or even to remove it; the acid should be applied by an applicator, round which a swab of absorbent cotton wool is rolled and cut short, in fact the cotton wool brush of ordinary use in throat practice. This treatment may with advantage be combined with the chlorine mouth wash, and periodical syringing of the throat with biniodide of mercury solution of moderate strength. Later we substitute the boric acid irrigations.

In the case of children, a confection composed of chlorate of potash with honey, is often of service locally, and no ill effects

have been recorded from its liberal use [Formula 8]. In adults, the sucking of ice is a grateful, refreshing, and efficient means of reducing hyperæmia, and of aiding the dissolution of the exudation. In the case of children, iced milk, sweetened with saccharin, may be substituted, and will often be taken greedily.

Post-nasal diphtheria, otherwise naso-pharyngeal extension of the diphtheric membrane, is indicated when exudation is seen on the posterior surface of the uvula, and confirmed, where feasible, by posterior rhinoscopy. The remedies already enumerated should then be applied, either on a suitably curved cotton-wool brush, or by a syringe, the nozzle of which has been adapted to the purpose of irrigating the post-nasal space (Fig. 57).

Nasal diphtheria.—Local medication of the anterior nares is indicated whenever there is evidence of extension of the exudation to the naso-pharynx, even when no membrane is seen in the anterior nares.

Allusion has also been made to the serious form of reflex dyspnœa that may occur when the nares are blocked. If this be due to the presence of membrane, we do not hesitate to remove shreds or plugs, or to pass even with some force a cotton-wool brush charged with menthol [Formula 12] along the floor of the inferior meatus from the front nostril. No trouble must be spared to keep the nasal choanæ patent. Nor must any fear of hæmorrhage deter us from this necessary procedure; should undue bleeding occur, it may generally be arrested by syringing the nostrils with an antiseptic solution at a temperature of not less than 100° F. [Formulæ 14 and 15].

Not infrequently, however, nasal respiration is impeded, without any extension of membrane in the nares at all, the obstruction being caused by the presence of adenoid vegetations, otherwise to an overgrowth and inflammation of the third or pharyngeal tonsil.

In such cases—short of operation, to be presently considered—we irrigate the nasal passages with an antiseptic and disinfectant lotion, either by means of a nasal syringe, the nozzle of which is perforated at five points (Fig. 58), or, better, by "Leffert's" coarse

spray, followed by the application of an oily solution of menthol, by means of an atomiser; to be alternated by the use of a disinfectant ointment, according to the practice of Dr. William Gayton, who has adapted Ward-Cousins' well known rectal ointment introducer for this purpose [Formula 22].

Laryngeal extension of the membrane should not only be sought for by careful examination with the laryngeal mirror, before respiratory symptoms give notice of its existence, but it should, at the earliest possible moment, be treated. Detailed

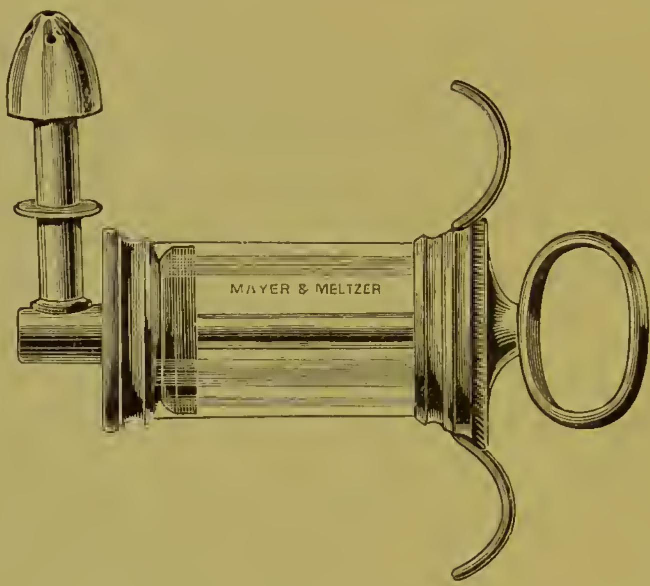

Fig. 58.—Anterior nasal syringe for diphtheria.

directions for combating this form of complication will be found in the next chapter.

Aural Diphtheria (acute median otitis), of which there is often no indication by pain, may not be realised until a suppurative discharge is seen to proceed from a ruptured drumhead. This is otherwise when the complication arises in connection with a pseudo-diphtheria, or with an attack in its true type, which may occur in the course of, or as a sequel to, scarlet fever or measles. Here pain is experienced, which gives definite warning of the mischief, and careful examination of the condition of the tympanic membrane should in such circumstances be made, since paracentesis being promptly performed would often avert destructive per-

foration leading to chronic otorrhœa. This procedure is to be viewed not only as a conservative measure against such an eventuality, but as essential to complete and effectual disinfection of the Eustachian tubes and tympanic cavities. This can be effected by syringing with a warm solution of boracic acid [Formula 20], either by the external meatus, or combined in some cases with anterior nasal irrigation with a similar solution. In either case Politzer inflation should be employed, so as to thoroughly clear the Eustachian tubes.

A very light and small pledget of absorbent wool soaked in a stronger solution of boracic acid, or other disinfectant, should then be applied to the membrane, and the meatus lightly packed with wool.

We are not in favour of dry insufflations, since they are likely to form dry crusts with the purulent secretion, which are not always easily removable. We have already given it as our opinion that an extension of the suppurative process to the mastoid cells is not very frequent in diphtheria, still less so is meningeal inflammation, but both are rendered less probable in proportion to the care displayed in the directions just given. Should there be redness, swelling, or tenderness over the mastoid region, with pain, not promptly relieved by Politzer inflation, an incision should be at once made down to the periosteum. Trephining of the mastoid is rarely called for.

Deafness resulting from diphtheria, the perforation having healed, may be due to intra-tympanic changes, or alternatively to a paretic condition of the muscles of the tube and tympanum, in which circumstance those remedies indicated for general sequelæ of this order should be employed.

Ocular Diphtheria.—In the very rare event of membrane forming on the conjunctivæ, Hermann Cohn, of Breslau, recommends as most efficacious, hourly pencillings with a 5 per cent. solution of benzoate of sodium, and declares that since he began to employ this treatment no patient affected with this form of diphtheria has lost an eye. Theoretically, therefore, this solution

should be also good as a faucial application, but the known effects of the salt hardly encourage us to urge its adoption.

The secondary effects of diphtheria on the eye, in the shape of pareses of the muscles of ocular movement and of accommodation, have always a strong tendency towards cure.

External Applications.—On the occasion of the International Congress in 1881, we made tentative recommendations of *Leiter's coils* for application of continuous cold in place of ice-bags. Since then, we have had oft-repeated testimony in our practice and that of friends and colleagues, of their great value in diphtheria as a means of applying constant cold without moisture. The effect is to reduce inflammation, and to favour rapid necrosis and separation of the exudation.

Hot applications to the throat in the way of poultices are cumbersome, wearisome, and, in our experience, unproductive of sufficient relief to compensate for their inconvenience; but, when pus has formed in the cervical or submaxillary glands, or an incision has been made, moist heat is indispensable.

Operative measures are generally supposed to be comprised in the procedures of *tracheotomy* and *intubation;* but it is now fully seventeen years since we first proposed and adopted the *removal of enlarged tonsils* and an elongated or thickened *uvula* during the *acute* stage of diphtheria. All who have any experience of the disease must be aware not only how prone are the subjects of enlarged tonsils to succumb to diphtheric attacks, but also to what a serious extent the existence of such a condition complicates matters, and imperils the chances of recovery. One must have seen over and over again oral and nasal respiration each hour more impeded from this cause, and for the same reason inspection of the larynx often made well nigh impossible. We therefore, in 1878, removed the tonsils of a child suffering from diphtheria on the first occasion of our visit. The result was an immediate improvement in her breathing: there was no extension of the disease to the larynx; the membrane was to some extent re-deposited on the cut surfaces, but it ultimately cleared; the child had several sequelæ of diph-

theria, but finally made a very good recovery. We reported the case in detail, and exhibited the patient at the Medical Society of London. Since that time we have had similar cases with an equally good result, and also others in which removal from adults of swollen and relaxed uvulæ during the acute diphtheric state has given notable relief.

We were not aware, when first adopting these operative measures, that Bouchut had been the first to pursue identically the same treatment, and that it had been condemned by Sanné in the following words:—"This practice should be classed with cauterisation. Its object is the same. It undertakes to destroy the mischief on the spot, and to prevent infection of the economy. The false membranes are said not to be reproduced upon the wound on the tonsils. Notwithstanding several fortunate cases reported by several physicians, this therapeutic method has had no result than to give a denial to the theory it should have sustained."

We, for our part, were quite prepared to hear the wisdom of the practice questioned on somewhat similar grounds; but however startling the procedure may at first sight appear, any objections which could be raised against it are theoretical rather than practical, and of no account in the balance, when weighed against its advantages—first, as removing an impediment to the respiration; secondly, as tending to prevent the downward progress of the exudation; and lastly, as an early substitute, or means of averting the necessity for, the more dangerous measure of opening the windpipe. The treatment has since then been adopted by, amongst others, Lefferts of New York, by John Macintyre of Glasgow, and also by our colleague, Mr. Percy Jakins, all of whom bear witness to its good results.

Dr. Watson, in an able graduation thesis, published in the *Glasgow Medical Journal*, July 1894, has rightly insisted on further reasons for this practice than that of relief of distress in breathing, and in fact many of them were in our mind when we spoke of the procedure as calculated to check the extension of membrane.

These further recommendations are—(1) that if the disease be limited to the tonsil—and we have seen in how large a proportion of cases it is confined to that situation—we can cut the infected part away; we know, also, that the specific bacilli are on the surface; so we should, by this procedure, at the same time remove them, and indeed, if the operation were adopted sufficiently early, before the toxic products have had time to be generated or absorbed to any serious extent.

(2) Antiseptic and germicidal applications would, by penetrating more deeply, have a better chance of arresting the systemic toxæmia and infection.

(3) The local depletion by bleeding is beneficial even beyond the region where it is induced. For even if the membrane has already spread to the larynx or nares, the removal of the enlarged tonsils or a swollen uvula cannot fail to diminish the dyspnœa.

The objections to this treatment which have been raised are,—that the membrane will re-form on the cut surface, which will be a particularly fertile soil for the growth of the bacilli, and that the lymphatics laid open by the tonsillotomy will allow a greater amount of absorption of the bacillary toxines than before; but neither of these objections seems to have been sustained by experience. On the contrary, by the test of thermometer, pulse rate, albuminuria, frequency and severity of paralytic sequelæ, &c., evidence is all in favour of the procedure.

The same remarks hold good in respect to the removal of *adenoids* causing great naso-pharyngeal obstruction and reflex spasm. Consideration of the relative merits and indications of *tracheotomy* and *intubation* is deferred to the next chapter.

CHAPTER XI.

LARYNGO-TRACHEAL DIPHTHERIA—CROUP.

Until the recognition of the Klebs-Loeffler bacillus as the material etiological factor of membrane, it was pardonable to consider that an exudative laryngo-tracheitis might be due to non-microbic causes. But since we are now in a position to state that membrane, due to other organisms, but identical in microscopical characters with diphtheria, may be deposited in the larynx as in the fauces, it is no longer permissible to speak of an idiopathic or catarrhal croup except as a condition so exceptional as practically to exclude it from our diphtherial nosology.

Hitherto the word Croup has been generally employed in this country as representing a pseudo-membranous inflammation of the larnyx and trachea, which, believed to be of a non-infectious and non-contagious nature, exhibits local rather than constitutional symptoms. But the term has now so long been used by Continental observers whenever an exudation extends from the fauces to the larynx and trachea, that to avoid further confusion, English authors would do well to accept this position. We may thus define **Croup as a pseudo-membranous exudation of the larynx and trachea, which may be classified on exactly the same lines as Diphtheria in the fauces**; we shall thus have:—

(1) Pure, simple, or bacillary Croup.

(2) Impure, complex, or cocco-bacillary Croup.

(3) Pseudo, false, or non-bacillary Croup.

Croup is rarely primary in the larynx, being usually exhibited as a downward extension of the membrane from the fauces, when it is called *descending*.

Cases without doubt occur in which there is apparently no evidence of direct extension of the membrane from the fauces, but our own experience leads us to believe that it is the rule whenever the larynx is involved; for we have never failed to observe a direct continuation in cases we have examined. In many instances the exudation will be seen to have commenced by creeping along the outskirts of the larynx from the lateral glosso-epiglottic folds. The epiglottis is almost invariably first attacked, and seldom escapes.

An *ascending* form of croup, otherwise an upward extension of

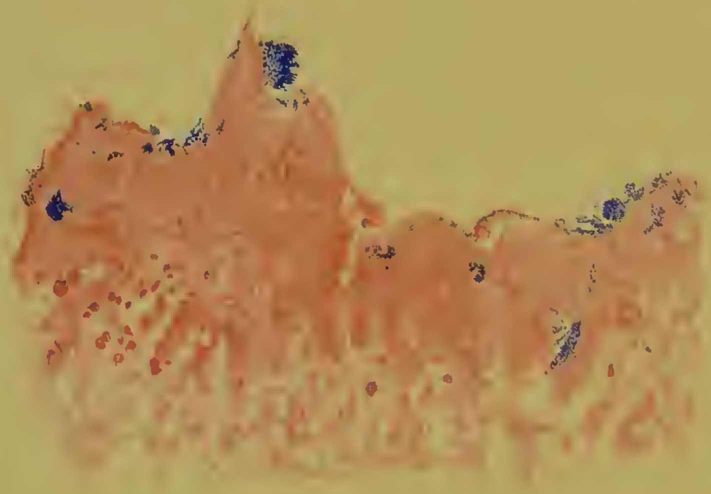

Fig. 59.—Non-Bacillary Croupous Membrane from the Trachea. Staphylococci with a few Streptococci *in situ*.

membrane from the bronchi to the larynx, has also been described, but it is difficult of proof. In any case it must be rare.

When non-bacillary, **Croup** has been asserted by Dieulafoy, in his *Pathologie Interne* (Vol. II., 1894), to be due to the presence of little cocci, which present themselves in groups of two, and from his description and allusion to their discovery by Roux and Martin, he evidently identifies them with the "Brison coccus" of those authors; but why pseudo-diphtherial croup should be attributed only to this particular micro-organism, it is somewhat difficult to understand, since these cocci play but an unimportant *rôle* in faucial inflammations. Dieulafoy further states that pseudo-

membranous laryngitis, due to strepto- and pneumococci, has no tendency to penetrate and grow in the larynx.

Klein and Councilman similarly select the streptococcus as the particular organism of pseudo-diphtherial croup, but the accompanying illustration of a false membrane in the trachea, from a beautiful preparation made by Dr. Taylor Grant while in Roux's laboratory, proves that staphylococci as well as streptococci (Fig. 59) may be responsible for the membrane, and may penetrate in exactly the same manner and to the same extent as the bacillus itself. Indeed, there appears no reason why, in the case of an extension of the membrane from the fauces to the larynx, the coccus should be assumed to change its type.

The following is a case illustrative of pseudo-diphtherial croup, of strepto-staphylococcal origin:—

F. H., male, aged 3 years. Admitted to hospital February 17th, 1895, at 7 P.M., having suffered from cough and sore throat since 14th. No fact could be elicited pointing to the possibility of a scarlet fever infection. Albumen was present, but at no time was more than a haze.

On admission, membrane was seen on both the tonsils and soft palate. Croupy cough and marked ensiform retraction suggested laryngoscopic examination, when membrane was seen in the larynx. 20 c.c. antitoxin (B. I. P. M.) injected.

Bacteriological examination, from cultures made on admission, showed strepto- and staphylococci, but no diphtheria bacilli. This examination being doubted, another was made on the 21st, but likewise failed to reveal diphtheria bacilli.

February 18th.—The temperature had fallen to 98·4. The breathing was easier and without stridor. Sternal retraction less marked. Exudation had neither diminished nor increased. Antiseptic irrigation also prescribed. Evening temperature 102°.

February 19th.—Temperature and general condition much the same.

March 3rd.—A rash was noted, which disappeared within twenty-four hours.

March 13th.—Death. *Necropsy* revealed the following:—Lower lobes of lungs airless, especially on the right side; evidences of bronchopneumonia in the middle lobes. A soft membranous exudation, extending from the lower surface of the epiglottis along the larynx and trachea, so as to make an almost complete pulpy cast of this tract. Similar membrane was seen to extend into the left bronchus.

We are inclined to agree with Fraenkel that non-bacillary croup may sometimes be infectious, especially when strepto- or staphylococci are present in the exudation, as also with the opinion of the same observer, that true diphtheria is liable to follow on a croup of an originally non-bacillary nature, more so, probably, than in the fauces.

The inflammations of the larynx, which take place as secondary results of some of the exanthemata and specific fevers, may also be non-diphtherial.

Sidney Martin, in 1892, expressed the opinion that "there is no evidence at present of any disease other than diphtheria which can produce a false membrane in the larynx."

Ruault, writing in the same year, believes that, in the great majority of cases, bacillary croup is consecutive to a true diphtherial condition in the fauces.

But Billings (1894) has found that of 286 cases in which the membrane was confined to the larynx and bronchi, 80 per cent. proved to be true diphtheria, only 14 per cent. being undoubtedly not diphtheria. This last view is in entire agreement with our own conclusions, not only as to fact, but to frequency.

These opinions and statements refer especially to those cases in which croup is due to micro-organisms; but false membranes of essentially the same macroscopic and microscopic character as those of truly diphtherial origin have been reported as produced on the mucous lining of the buccal cavity and air-passages by every kind of traumatism, as, for example, irritant poisons, solid, fluid, or gaseous, scalding water, scorching heat, chemical or galvano-caustics, or even strong Eau-de-Cologne. Oertel performed the experiment of dropping a few minims of liquor ammoniæ into the trachea of seventeen animals, and succeeded, in every instance, in generating an artificial croup.

There are still many practitioners, whose opinions are entitled to respect, who hold that croup may be the result of exposure to atmospheric causes, such as intense cold, and quite independently

of any microbic infection, but in the light of advanced bacteriology both traumatic and atmospheric causes must, in the future, be held to be only predisposing.

With regard to the morbid anatomy of **non-bacillary** croup, a special distinction has been made that in true diphtheria the exudation is poured out, not only on the superficial portions of the mucous membrane, but that it also invades and penetrates the lymphatic spaces, and so reaches the deeper parts of the regions attacked: Weigert has enunciated that in true diphtheria the deeper tissnes are involved in a necrotic process.

Our microscopic sections hardly warrant us in accepting these distinctions as of uniform application.

In the supra-glottic region, false membranes are as firmly adherent as those in the fauces, but they become thinner and less adherent the lower their site in the air-passages. In the minute bronchi they are almost fluid. The bacilli and other organisms also become less numerous.

Our position with regard to the pathology of croup having been thus defined, further remarks will be directed to such changes in the symptoms and treatment as shall depend on anatomical site and its inhibitory influence on the performance of vital functions.

Symptoms.—The onset of primary croup may be heralded by those general prodromata common to diphtheria of the fauces, but more usually croup occurs as an extension from the fauces, to be witnessed on the third or fourth day. The difference in situation results in functional disturbance, which, according to Barthez, may be divided into three successive stages, the first characterised by cough and hoarseness, the second by aphonia and paroxysmal dyspnœa, and the third by suffocation and asphyxia, ending in death. Between all these there is no hard and fast line, and indeed very many cases never go beyond the first stage, in which circumstance Ruault employs the term *abortive croup.*

Croup begins with a small, dry, and frequent **cough**, which has a high-pitched, metallic, and ringing sound, generally denominated

brassy and laryngeal, but is liable to become gradually muffled and even noiseless.

Change in the **voice** is another and sometimes the first symptom. Beginning as a simple catarrhal hoarseness, it is soon observed to assume a metallic timbre and to be raised in pitch. When membrane is abundantly manifested on the cords, complete aphonia may ensue. This phenomenon may also be explained by paralysis of the adductors. This may be merely functional, or due to diphtherial neuritis and myopathic changes.

Sometimes there is slight **pain** in the region of the larynx. Embarrassment of respiration quickly supervenes, the movements increasing in rapidity to thirty-five or even forty per minute.

There now occur attacks of paroxysmal **dyspnœa** of the most painful and alarming character, and these may commence so soon as a few hours after the first warning that there is anything wrong. Each inspiration is attended by a peculiar stridor, which constitutes one of the most marked characteristics of the disease. This stridor has been variously described as high-pitched, piping, shrill, metallic, sibilant, and wheezing. During the dyspnœa there is indrawing of all the muscles of the supra- and sub-sternal regions, as also of the epigastrium, the false ribs, and even the lower portion of the sternum itself; of all those parts, in fact, which would generally be distended in healthy inspiration. All the inspiratory muscles, regular as well as auxiliary, are observed during the spasm to work painfully; the dilated nostrils, the terrorised expression of the face, and convulsive movements of the limbs, all giving evidence of a laborious and futile struggle for breath. The complexion becomes cyanotic, and death from apnœa appears imminent and may even occur. Should membrane be coughed up there may be a favourable termination to the dyspnœa, when the metallic sound of the cough will be observed to change to that of a bronchitis or remitting laryngitis.

Diagnosis.—Independently of the question of membrane in the fauces, the history of the attack, the absence of fever and cough, and the complete remission of all symptoms between the attacks

which distinguish laryngismus stridulus, and the reflex cough observed in some cases of enlarged pharyngeal and faucial tonsils, are sufficient to prevent the graver malady being mistaken for the milder.

Laryngoscopic signs.—In a case of average acute type, the larynx presents, at the onset, a diffuse red colour of varying intensity, and with some tumefaction of the mucous membrane. Later, there are seen here and there on the epiglottis, the ary-epiglottic folds, the inter-arytenoid commissure, ventricular bands, fine pellicles of membrane, which is at first of a brilliantly opalescent white (*see* Frontispiece). These become yellow or greenish in colour, and thick and opaque, with a tendency to spread over the greater part of the laryngeal vestibule, and finally to reach the vocal cords and the sub-glottic region. In other cases the larynx may be seen to be simply red, and to exhibit only a minute quantity of membrane, whilst the sub-glottic region and the trachea, so far as can be seen, are more or less entirely covered by fibrinous exudation. Failure to discover membrane in the larynx by no means implies that there is no exudation in the infra-glottic region. Often in examining a faucial diphtheria the membrane may be seen extending to the free edge of the epiglottis and no further; but these cases, as a rule, give no trouble from laryngeal symptoms. In others, considered to have arisen primarily as laryngeal, membrane may have cleared away from the fauces before the air-passages have been attacked.

Bretonneau attributes the cause of the **dyspnœa** to the mechanical obstruction of the exudate in the larynx; Jurine, author of Napoleon's prize essay, to a spasm of the glottis caused by the irritation of the laryngeal mucous membrane; Cadet de Gassicourt to a paralysis of the dilator muscles and to the action on the medullary centres of the de-oxygenated blood. Ruault is of opinion that Jurine's view is alone justified.

No doubt both the extent and density of the membrane plays a very important part in the obstruction, but a very small and thin pellicle of exudate is compatible with much dyspnœa and spasm

Such a case quite recently occurred in the hospital practice of my colleague, Dundas Grant.

Actual nervo-muscular laryngeal paralysis is an exceptional, and cannot be considered the usual cause of dyspnœa, but when it does occur it probably involves the *abductors* rather than the *adductors*, because loss of phonetic quality is by no means uniformly synchronous with extreme dyspnœa, unless the vocal cords are themselves the site of membrane. The nasal voice, due to palatal paresis, is to be distinguished from changes in primary laryngeal tone. Not that we deny that the adductors are also and, indeed, mainly implicated, and this is often the cause of the aphonia, but in such case the respiratory difficulty is purely spasmodic, and consequently of a less dangerous character. Even when the dyspnœa appears to be entirely due to a mechanical obstruction of the air-passages by membrane, spasm is always superadded. Administration of chloroform during an attack of dyspnœa bears out this idea, as under its influence the dyspnœa diminishes or even disappears altogether.

Of **complications** due to croup, *acute bronchitis* is very common. *Pseudo-membranous bronchitis* is rare, or perhaps one might say difficult of recognition, during life, since stethoscopic signs are uncertain; the only sure sign of membranous extension to the bronchi is the expectoration of ramified casts of the tubes (Fig. 60), but, as previously stated, diphtherial exudation diminishes in fibrinous quality the lower it descends, and is often found to be of almost fluid consistence in the smaller bronchi.

Broncho-pneumonia is to be recognised by well-known signs, and may generally be interpreted as evidence that the croup is either pseudo or complex diphtherial in character.

Prognosis, course, and termination.—Even mild attacks of croup should give cause for anxiety, for neglect of a simple case has frequently been followed by relapse of the malady in an aggravated form, with a suddenly fatal termination. Age is an important element in prognosis, and the older the child the more favourable is the chance of recovery.

The general elements of prognosis in faucial diphtheria apply equally to the laryngo-tracheal form, in which, however, there is an added danger of no little importance—viz., laryngeal obstruction. When croup does not extend beyond the vestibule, it may remain latent, and recovery take place without having given rise to any symptom of distress, and even when it has advanced so far as the inter-arytenoid space, spontaneous cure is still possible, and such recoveries occur to the probable extent of 5 to 10 per cent.

FIG. 60.—TRACHEAL and BRONCHIAL CASTS, from a Case of Diphtherial Croup.

When the membrane extends further, and there is paroxysmal dyspnœa and aphonia, spontaneous cure rarely, if ever, takes place. But surgical intervention distinctly diminishes the mortality.

In the course of the disease towards restoration to health, gradual separation of the membrane takes place, followed by free mucous expectoration, and diminution in the severity and stridulous character of the cough and respiration.

In milder cases there may be no objective evidence at all of

membrane in the expectoration, the exudation having either not arrived at the stage of fibrinous deposit, or having become pultaceous before release.

The duration of a case in its acute form is from four to ten days; complete recovery being delayed to a month or five weeks, and in some instances being followed by one or more relapses.

When the disease takes an unfavourable course, the paroxysms become more frequent and almost unremitting; the cough, although toneless, is more distressful; the pulse-beats are more rapid, the little patient is more restless, and the extremities become cold; finally they, as well as the countenance, become cyanotic.

The fatal issue may occur in any of the following ways: by *apnœa,* or by *convulsions* during a paroxysm of dyspnœa; by *asphyxia* through actual blocking of the air-passages with membrane, otherwise *carbonic acid poisoning;* by *cardiac failure,* due to diphtherial toxæmia or to deposit of *fibrin* in the *heart* and great blood vessels; by *exhaustion and coma;* and finally, by *secondary lung complications.* The date of a fatal termination is seldom extended beyond the fourth or fifth day, unless tracheotomy has been performed, in which case, even if life be not saved, death may be somewhat delayed, and is more peaceful.

Regarding the convulsive nature of the paroxysms, Ferriar (1798) has reported a case in which the struggle was so violent that after death, the corpse, in a great measure, rested on the occiput and on the heels.

Treatment of Croup requires to be pursued with energy and discretion from the first.

There is a general consensus of opinion in favour of an atmosphere hyper-saturated with steam; but we are inclined to think that this treatment is often carried to excess.

The bed should be curtained, and vapour brought near it by means of a steam-kettle, but the croup tent bed, which gives the little patient a continuous vapour-bath, is as unnecessary as it is depressing.

If vapour is required to be brought nearer to the child's mouth, that purpose is best effected by a steam draught inhaler with plain water impregnated with pinol [Formula 23], or in the case of spasm with benzoin and chloroform [Formula 24].

This desideratum may be enhanced by the general inhaling of carbolic acid vapour from a steam-kettle placed near the bed, so that the patient may be said to live in such an atmosphere night and day. But as children are very liable to carbolic acid poisoning, the effects on the urine should be carefully watched, or pinol, eucalyptol, or terebene be substituted.

This measure, combined with internal administration of sedatives to allay spasm, is in many mild cases all that is required.

In infants it may be impossible to apply local remedies to the membrane, except by a cotton-wool laryngeal brush introduced by guess work; but in those older, by help of the laryngoscopic mirror and after the use of cocaine spray to allay spasm, one may sometimes be able to detach it and apply strong antiseptic solutions.

Of general measures of traditional repute there is, however, much to be said in favour of an emetic given at the first onset of an attack, and it is indicated on the ground that should membrane be formed in the trachea or bronchi, as is not unfrequently the case before the manifestation of laryngeal symptoms, an emetic may possibly favour its expectoration; and even later when the larynx is covered with membrane the action of an emetic may help to detach pieces of it which are only slightly adherent.

But a more profound reason for the salutary action of such an emetic as ipecacuanha is its moderately depressant effect, by which reflex excitability and laryngeal spasm are diminished. But the main indication for this remedy should depend on the bacteriological examination, and should be contra-indicated where the diphtherial asthenia is at all pronounced; in any case, it should only be employed in the early stages of the attack.

The best form of emetic for a child from one to five years of age is a teaspoonful of ipecacuanha wine every fifteen minutes till vomiting is produced.

The further general and constitutional treatment of croup is to be carried out on exactly the same lines as in faucial diphtheria. The cough and spasm should be allayed by chloral and ipecacuanha [Formula 6]; inhalation of chloroform may be necessary in violent spasm.

Of further local measures we prefer the continuous external application of cold by the Leiter coil, already advocated in the faucial variety. This application does not allow cold moisture to drip down the neck and chest, nor does it damp the night-dress and sheets as do cold cloths, or ice-bladders. On the other hand it is quite as easily retained as a poultice or stupe or sponge, and in the more recent form of its inventor is of no great weight. Whether for the purpose of reducing the inflammation, of modifying the spasm, or of favouring rapid separation of the membrane, application of continuous dry cold is preferable to that of *moist* heat, which is almost always followed by chill. Should warm applications, however, be preferred to cold, they can equally well be applied by the coil.

We do not any more prescribe applications of solutions of nitrate of silver, so strongly recommended by Bretonneau, Niemeyer, and other older writers, nor indeed any other mineral solution; for, however mild, such applications, especially the first-named, are provocative, not only of spasm, but of coagulation of the ordinary secretions of the mucous membrane. The use of the croup brush is also to be carefully avoided, unless the practitioner is *quite prepared to perform tracheotomy immediately afterwards,* for the forcible disturbance of membrane in small children is very apt to block up the narrow glottic chink, and so to lead to serious and even fatal suffocation, and this quite apart from the dangers of spasm. The same caution is to be observed in relation to attempts at *intubation,* which will be considered presently at greater length.

Operative Measures for the Relief of Croup.

We have considered the question of the removal of enlarged tonsils, uvulæ, and nasopharyngeal adenoid growths in our chapter on faucial diphtheria, but in laryngo-tracheal cases some other operative procedure is required to prevent death by asphyxia due to mechanical obstruction in the larynx. Which is it to be, Intubation or Tracheotomy? To decide this, the first step is to make, if possible, a laryngoscopic examination, which alone can give us an adequate idea of the extent of surface involved; and if the laryngeal mirror, as we have all along contended, is advisable in case of diagnosis, it is indispensable when deciding on an operation, and it is not unnecessary to repeat that only those in the habit of using it are in a position to appreciate how much aid it can afford.

One may rarely fail to see whether membrane is or is not in the larynx, and to what extent. The "gagging"—which introduction of the mirror induces in young children who are the subjects of enlarged tonsils—is even an advantage in affording a complete, albeit only momentary, view, of which the expert will not be slow to avail himself.

Success in the treatment of croup does not depend on the number of tracheotomies or intubations, but rather on the number of favourable results which are obtained without operation; and the more expert the practitioner is in the use of the laryngoscope, and the more skilled in making intra-laryngeal applications, the smaller will be the number of occasions on which he will require to resort to operative procedures.

Examination with the mirror may reveal the presence of only a small piece of membrane removable by the laryngeal cotton-wool brush, the hand being guided by the reflector. Such a manipulation ought to be preceded by spraying the throat and larynx with a 5 to 10 per cent. solution of cocaine to allay spasm, and should be followed by the use of benzoin and chloroform

inhalation [Formula 24]. No operation whatever may be required should the foregoing procedure be happily effected.

On the other hand, there may be noticed a redness of the vocal cords without much membrane in the glottis, in which case intubation would relieve the associated spasm; or such an amount of membrane may be seen on the cords and below them as to contra-indicate intubation and to demand tracheotomy.

Other data have to be considered before we can decide whether to intubate or to open the windpipe.

From the standpoint of statistics one cannot give preference to one or the other, except that in children under four years intubation is probably a more successful operation. The question is, which is the more simple and more easily executed, and what are the advantages and inconveniences of each?

Even in experienced hands, difficulties often occur in the introduction of the intubation tube which may equal those of tracheotomy. Not infrequently it has been found necessary to perform tracheotomy after intubation, because the latter may fail to afford relief to the embarrassed respiration, or it may be found impossible to nourish the child properly; and the operator should be forearmed against this eventuality, having ready the necessary intruments for an immediate tracheotomy in case the intubation tube cannot be introduced, or if, in the very act of introducing the intubation tube, membrane has been pushed down so as to block the respiratory tract. And the same precaution should be observed when proceeding to withdraw an intubation tube from the larynx, often an even more difficult operation than the introduction, so that it would be well that the instruments for the two operations were always carried in the same case.

A point not in favour of intubation is the fact that the removal and re-introduction of the tube requires skilled hands, whereas the nurse may remove, cleanse, and replace the tracheotomy tube.

In hospital practice, where everything is ready and skilled assistance at command, there is more to be said in favour of intubation than there is in private practice, in which these difficulties

rather prevent intubation from becoming a formidable rival to tracheotomy.

After intubation there is usually, as already premised, trouble in deglutition, but this difficulty may be overcome by giving food of a semi-solid consistence and in a particular manner to be presently described.

False membrane and mucus from the trachea is expelled less easily in intubated cases, and the tube is liable to blocking by exudation drawn upwards into it on coughing; but this latter accident is quite as probable in the case of tracheotomy. It is, however, more easily overcome by the simple removal and cleansing of the inner tube, which can be done by the nurse, at the same time clearing the trachea by long forceps or feather. In intubation, removal and re-introduction of the intubator when necessary may be unduly delayed in adoption, since being more intricate it requires technical skill. In almost any case, and especially where there is a large amount of exudation or mucous secretion, the intubation tube may require to be removed at least daily for the purpose of cleaning.

The operation of tracheotomy gives functional rest to the larynx, and permits a more thorough clearing away of membrane and more efficient medication of the regions both above and below the tracheal opening. And not the least valuable point in favour of tracheotomy is the access which it gives for the application of solvents such as lactic acid, disinfectants such as biniodide of mercury, or liquefiers of mucus such as bicarbonate of sodium, whereas intubation is actually adverse to employment of these valuable auxiliaries.

In view of the tendency of the diphtherial poison to attack peripheral nerve tissue, especially of those muscles which are most in use, and in the order of vital importance, it is probable that the occasional ulcer caused by pressure of the intubator is a direct result of paralysis and degeneration of the laryngeal muscles.

In very young children, under four years of age, intubation has given better results than tracheotomy. Stern's statistics show

that under three and a half years, intubation gives a decidedly larger number of recoveries. Being a bloodless operation, and not requiring an anæsthetic, the consent of parents is more easily obtained, and thus children are saved who would otherwise die owing to inability to obtain the parents' consent for tracheotomy. For a similar reason the operation can be performed earlier, before the patient is moribund—as too often happens with tracheotomy. Finally, for the poor in their own homes it is decidedly superior to tracheotomy. The tracheotomy tube requires constant and even skilled attention, whereas the intubation tube in cases suitable for its employment may often be allowed to take care of itself.

TRACHEOTOMY.

This is a procedure which is each year viewed more favourably, mainly because the indications for its performance are becoming better appreciated, and we are now able to assure the relatives of a patient that, when adopted sufficiently early, the chances of success are much greater than formerly.

The indication for operative interference, whether tracheotomy or intubation, is the occurrence of *progressive asphyxia* as evidenced by the suppression of voice, increasing dyspnœa, stridor, cyanosis, and especially by the retrocession of the chest walls. When on auscultation the vesicular murmur is not clearly heard, but in its place the inspiratory laryngeal sound, there should be no delay in operating, though an attempt should always be made to verify the cause of the symptoms by the physical signs as capable of detection by the laryngoscope. There are, indeed, no contra-indications for tracheotomy once its necessity is indicated, and the sooner it is done before exhaustion sets in and the system is loaded with toxines the greater the chance of success. The younger the child the less should be the delay. Another reason for early operation in laryngo-tracheal diphtheria is its well known tendency to spread downwards, and thus set up a serious membranous bronchitis.

In our series of 1000 cases of diphtheria, we find tracheotomy was performed by Dr. Gayton, the medical superintendent, and his assistants, in 68 instances. Of these 34 died and 34 recovered. Of the 34 fatal cases, membrane was present in the larynx alone in 2; in the fauces and larynx in 23; and in the fauces, larynx, and nares in 9 instances.

In the total number of 68 patients on whom tracheotomy was performed:—

In 3 cases membrane was present in the larynx.
„ 49 „ „ „ fauces and larynx.
„ 16 „ „ „ fauces, larynx and nares.

The percentage mortality for site is:—

Larynx, ...	66·6.
Fauces and larynx, . .	46·93.
Fauces, nares, and larynx, .	56·23.

Total mortality, 50 per cent.

In support of the value of tracheotomy, Dr. Gayton points out that since greater reliance has been placed on this procedure the death rate from diphtheria at the North-Western Hospital has been reduced from 31·42 to 26·48 per cent., including those very numerous cases which, admitted in a hopeless condition, die within 24 hours. If these were deducted the mortality would be reduced to 22·6 per cent.

Dr. Gayton concludes the valuable paper from which these remarks are taken by saying that "beyond all question many lives may be saved by an early resort to opening the trachea." Especially is this so in that class of case in which the strength is maintained, but in which the danger is death from asphyxia.

As to the risk of pulmonary complications, and, in particular, broncho-pneumonia, to which a useless tracheotomy would expose the patient, we do not think we are justified in making that an argument for delaying tracheotomy to the last moment.

Early tracheotomy is, then, more advantageous than late tracheotomy. In other words, one need not wait till there are

pronounced signs of asphyxia, but, on the contrary, should act as soon as there is slight suffocation and dyspnœa. Another advantage of this practice is to spare the patient not only hours of anguish, but much emotion and pain. Besides, the early operation not being suddenly called for is carried out under anæsthesia, is done without hurry, and in every respect under the best possible conditions.

If even before occurrences of respiratory signals of distress membrane can actually be seen in the larynx by means of the mirror, no delay should be allowed to occur, and the advisability of opening the windpipe should be promptly urged. We do not advocate its performance where the chances are, from excessive toxæmia or septicæmia, hopelessly unfavourable, because knowledge of fatal results tends to influence parents in their refusal under circumstances which are perhaps most favourable. Nevertheless, it is noted that in many cases in which death occurs after tracheotomy, the operation gives some days or hours of quietness, and the end is much more tranquil than would otherwise have been the case. We must always consider this operation principally with regard to children, in whom death by mechanical obstruction is much more frequent than in adults. In the latter, tracheotomy is far less frequently called for, and it would appear is less successful than in children, probably because the dyspnœa when present is not so purely mechanical in its nature.

The scope of this essay does not call for any great details as to the performance of tracheotomy. These are to be found in all surgical text-books. The operation itself, though an easy one in the adult and in chronic disease of the larynx, is, on the other hand, full of difficulty (in so acute a disease as diphtheria), and in the very young, on account not only of the spasm, but of the depth at which the trachea lies in the case of a fat child, the shortness of the neck, the relatively large size of the thyroid isthmus, and, up to the age of about fifteen months, the possible presence of the thymus gland.

We may further note that it is well to make the operation as

far as possible a bloodless one by discarding the knife after the skin incision is made, and separating the soft parts by means of dissecting forceps.

The trachea should not be opened until its rings are clearly exposed and made free of all superposed tissue. We are in favour of a moderately high tracheotomy, and always endeavour to cut below the first and, if possible, the second tracheal ring.

A point by no means unimportant is to make a sufficiently long skin incision, and it may be added that all blood vessels should be doubly secured by forceps before dividing them. We are not in accord with those who put in the tube before bleeding has stopped, in the belief that once the tube is introduced hæmorrhage will be arrested. That way danger lies.

Anæsthesia.—A local anæsthetic, such as cocaine hypodermically employed, may be permissible and even advisable in the case of adults, but for children and for diphtheria we recommend a general anæsthetic, however late the stage of the disease; even in an emergency, when, as has been taught, there is no time for its administration, for the chloroform allaying spasm diminishes the immediate danger. There always is, indeed, less risk of the anæsthetic doing harm than there is from undue spasm, unrest, and constant upheaval where it is not employed. To this rule there is hardly an exception.

Chloroform is far preferable to ether, which is, indeed, contra-indicated from its liability to induce rather than to allay spasm of the glottis.

The operation over and respiration re-established, a successful result largely depends on careful nursing of the patient, careful cleansing of the tube and dressing of the wound, together with the observance of strict hygienic precautions. The temperature of the room should be kept constant, and the carbolic or other vapour kept playing continually to moisten and sterilise the atmosphere. Caution, however, must here be given lest the spraying be overdone by being too hot and abundant, and thus lead to greater depression and consequently to a greater liability to pneumonia

The spray should be small in quantity and cool in temperature. The inhalation facilitates detachment of membrane, and it may be said that in cases where there is only a small quantity of mucus secretion in the trachea more steam is indicated than when the secretion is abundant, this latter condition being rather a favourable sign.

The after-treatment consists in covering the wound under the tube with an antiseptic dressing, such as blue gauze, and the same to be lightly laid over the orifice. We are also in the habit of having a woollen pad with antiseptic gauze-covering laid over the chest to preserve from damp and cold arising from sprays, steam inhalations, &c. Biniodide of mercury (1 in 4000) is sprayed over and around the wound every two hours. Should the tracheal mucus be scanty and tenacious and difficult to expel, an antiseptic alkaline lotion (Formula 14 or 15) may, in the alternate hours, be applied by the atomiser through the canula, thus favouring a moist condition of mucus—not of membrane—and making expectoration more easy. After tracheotomy in favourable cases there is high temperature for 48 or 72 hours. Cough aids the expulsion of mucus and membrane, and, indeed, it is often of great utility to tickle the trachea by means of a feather charged with dilute lactic acid, thus simultaneously exciting cough and softening and removing membrane. The inner tube should be removed every one or two hours, cleansed, disinfected, and re-introduced.

The tracheal opening is to be regarded not only as affording relief to an obstruction in the natural breathway, but also, and most importantly, as a preliminary to adoption of measures for clearing the air-passages of such membranous obstruction, and the practitioner must not neglect continuance of persevering efforts in that direction, and in such local medication as may prevent exudative re-formations; but failure to always effect this end, as proved by the presence of membrane in the trachea in a fatal case of membranous laryngitis after tracheotomy, must not be regarded as any evidence of the want of due care on the part of

the surgeon in charge, as has been suggested by an author on this subject.

With regard to removal of the membrane through the tracheal opening, attempts to this end by oral suetion either of doctor or parent ought not to be neeessary in these advanced days of meehanical aids. One very simple instrument for the purpose is that of a Siegel's exhausting syringe, such as is employed in aural practiee, with a strong exhausting soft rubber bag to effect suction and the aural end adapted to the mouth of the traeheotomy tube by means of the aspirator, known as Coudereau's. By this instrument, made for us by Messrs. Krohne and Sesemann, not only ean exudation be extracted, but by a very simple contrivance, familiar to all who use aspirators, fresh air or hyper-oxygenated air ean be introduced into the lungs almost instantaneously after the extraction. An atmosphere of steam is more necessary after tracheotomy than beforc, sinee it is most important to guard against the oecurrenee of fresh inflammation due to inspiration of insufficiently tempered air by the tube.

One other hint hardly neeessary to experts. In removing membrane through a tracheal eanula, it is better to clear it by the inner tube, so that in ease that passage is blocked freedom ean be given to respiration through the outer canula. A double canula, always of value in tracheotomy, is of indispensable importance in eases of diphtheria.

At the end of twenty-four hours, the canula should be removed and replaced by another of the same size and shape, and this procedure should be repeated at least once a day until the tube is finally removed. Before this last step is taken, the tubes should be removed for a gradually increasing period of from four to eight hours. The withdrawal of the canula often occasions expulsion of much membrane and mueus.

The constitutional treatment should be eontinued, namely, iron and chlorate of potash, and the indieations for alcohol already given should be diligently observed. The ehild should not be overfed, a small quantity every two or three hours is sufficiently often, and

it is a point worthy of notice that soft semi-solid food is more easily swallowed than liquid. Feeding by the œsophageal tube may require to be resorted to.

The possible complications after tracheotomy are peri-tracheal cellulitis and abscess, emphysema, erysipelas, membrane on the wound, gangrene, and broncho-pneumonia.

The last is by far the most frequent cause of death after tracheotomy, a less frequent cause being cardiac failure, and still less, membranous bronchitis. The other complications are, no doubt, largely due to lack of antiseptic details. According to Cadet de Gassicourt, the cases of broncho-pneumonia which get well are those which appear from five to eight days after the operation, whereas those which follow tracheotomy in one or two days usually terminate fatally.

Intubation of the Larynx.

This procedure for relieving laryngeal dyspnœa by introducing a tube through the mouth, and placing it in the larynx with its upper end below the epiglottis, was first adopted by Bouchut in 1858; but the credit of re-introducing and gradually perfecting the instruments and method now in use must be assigned to Dr. Joseph O'Dwyer, of New York, who commenced his experiments in intubation in 1880.

We have mentioned some objections which render it doubtful whether intubation can ever entirely supersede tracheotomy, but without doubt there are many cases in which it may, at any rate, be adopted as a preliminary, and in not a few as a substitute. The operation has been performed extensively in America and to some extent in this country, and has been successful in very young children, the very class, in fact, in whom tracheotomy has given the least favourable results. We had the opportunity of seeing some cases at Chicago under the care of Dr. Waxham; we have since had some encouraging experiences of the operation in our own practice, and we are bound to confess that many former

objections which we entertained have been almost entirely dissipated; and in a communication read at the meeting of the British Medical Association at Glasgow in 1888, we stated somewhat fully our mature views on the subject, which further experience has confirmed.

The vast difference in the frequency with which the operation has hitherto been performed in America and in this country is no doubt partly due to the greater prevalence of diphtheria in America. It is probable, however, that the laryngeal mirror not having been used in the majority of cases, for the purpose of forming an exact diagnosis of the condition of things, the operation may have sometimes been performed for mere spasm, and before membrane had extended to the glottis. In any case, it is unquestionable that some of those who have had the largest number of cases of intubation in America are not laryngologists, nor expert with the laryngoscope. On the other hand, a large number of cases have been recorded by Roe, Ingalls, Casselbury, Stern, and Bleyer, to the nature of whose cases such an objection could not possibly be advanced.

A set of intubation instruments as now generally sold consists of five *laryngeal tubes*, together with a *gag*, an *introducer*, and an *extractor*. A scale is also supplied indicating the length of the tube suitable for a particular age. The tubes are made of brass plated with gold, and vary in length from $1\frac{3}{8}$ to $2\frac{1}{2}$ inches. The calibre of the largest tube is about $\frac{1}{4}$ by $\frac{1}{8}$ inch, and that of the smallest about half that size. The upper end of the tube is expanded into a head, which rests on the ventricular bands and prevents the tube slipping down into the trachea. The anterior part of the head is levelled off so as not to press on the base of the epiglottis. There is a small hole near the anterior part through which a thread can be passed. In the middle of its length is a fusiform enlargement by which the tube is retained in the larynx. Each tube is supplied with a so-called obturator which is inserted into the tube, and fits the openings accurately at each end. In the upper end of the obturator is a small hole by which it can

be screwed on to the introducer when the tube is about to be used. At the distal end the obturator projects slightly so as to form a probe-pointed extremity, which diminishes the risk of injuring the parts during introduction. The introducer consists of a handle and a shank, bent at its distal end at a right angle. To this end the obturator is screwed on, and, by pressing a button in the upper surface of the handle, two claws may be made to project down-

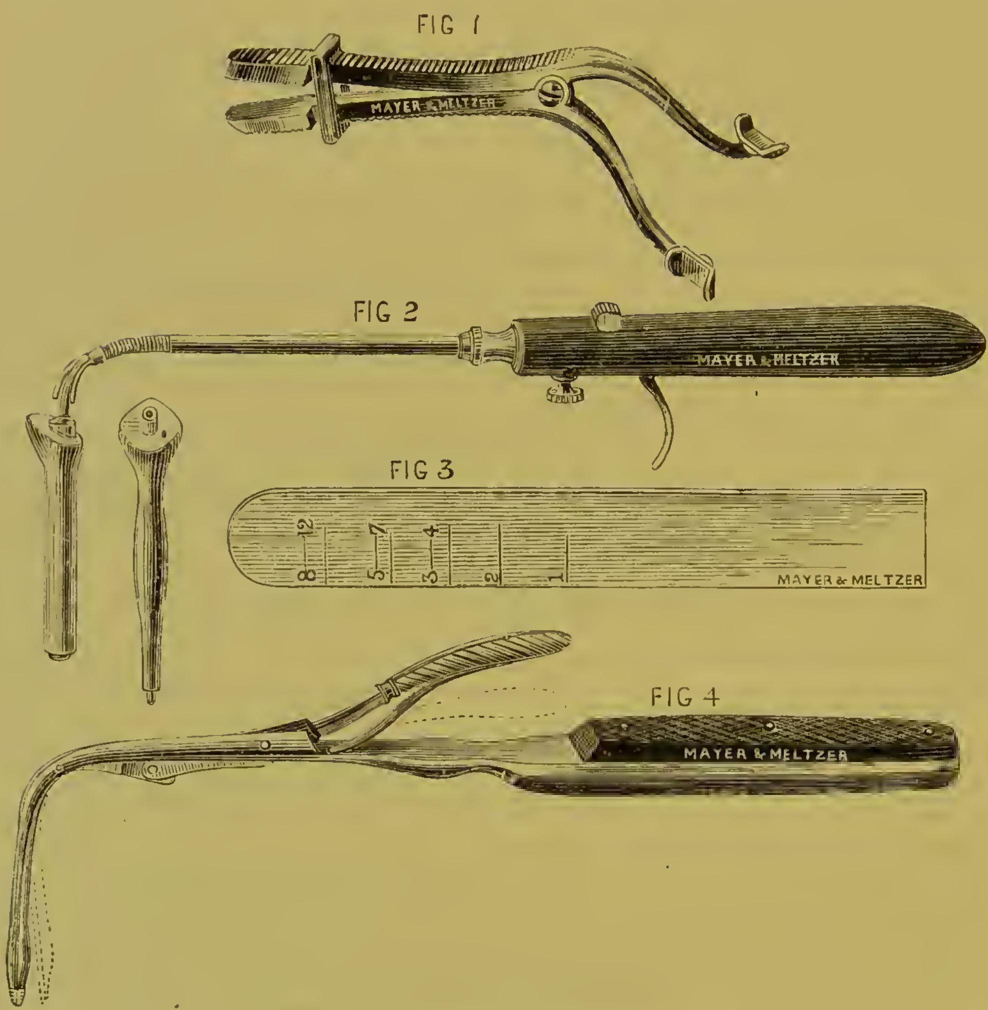

Fig. 61.—Intubation Instruments.

wards on the head of the tube, so as to push it clear of the obturator, and to allow the introducer with the attached obturator to be withdrawn when the tube is in position. The extractor is a curved instrument, at the distal extremity of which two small blades can be made to dilate by pressure on a spring in the handle. The extremity is inserted into the tube with the blades closed,

when pressure on the spring causes the blades to open, and the tube to be firmly held.

In *performing intubation* the first step is to select a tube suitable to the age of the child, which may be done approximately by reference to the scale. The tube is threaded with a piece of braided silk some sixteen inches long, the ends of which are tied together. The obturator is then screwed on to the introducer, and the tube is fitted on to the obturator. The nurse, seated upright in a straight-backed chair, takes the child in her lap with its back pressed against the left side of her chest, and its head thrown slightly backwards, resting against her left shoulder. She passes her arms round the child, and crosses its forearms in front and holds the wrists tightly, and if necessary she secures the child's

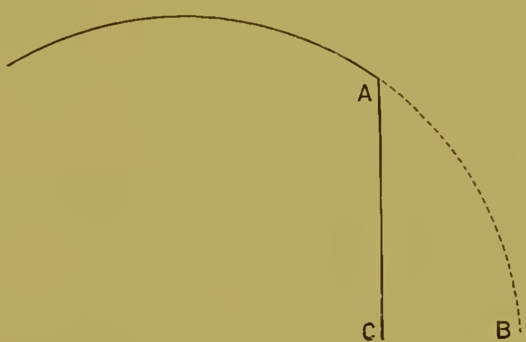

FIG. 62.

legs between her knees. The gag is next placed well back at the left corner of the mouth, and an assistant, standing behind the nurse's shoulder, holds the gag and steadies the head between his hands.

The following are the directions usually given:—The operator, standing or sitting in front of the child, takes the introducer in his right hand and hooks the loop of thread round the little finger of the left hand. He then rapidly passes the index finger of the left hand over the tongue and behind the epiglottis till the upper orifice of the larynx is felt. With the handle of the introducer held close to the patient's chest, the tube is introduced into the mouth and passed back over the base of the

tongue, guided by the index finger, and kept as nearly in the middle line as possible. When the point of the tube reaches the epiglottis, an abrupt turn is given to its course by raising the handle of the introducer, and thus bringing the tube into a vertical position. The tip is then passed into the larynx along the palmar surface of the guiding finger. As soon as the tube is in the larynx it is detached from the guide by pressing forwards the button on the handle, and as the guide with the attached obturator are withdrawn, the tube is pressed down with the tip of the left index finger until its flange is felt to rest on the ventricular bands, when the finger is at once withdrawn.

Fig. 62, which is taken from Dr. Waxham's book, represents the curve that should be made by the end of the tube while it is being introduced, the dark line indicating the path it should follow. If the point of the tube be continued in the curve as indicated by the dotted line, it will invariably enter the œsophagus.

The entry of the tube into the larynx is indicated by violent coughing, quickly followed by easy breathing. We have been astonished by the rapidity with which the bases of the lungs are aerated, and if there is any doubt as to the position of the tube the surgeon's ear applied to the back of the little patient will often settle it. If the instrument has passed into the œsophagus there is no violent coughing, and no relief is given to the breathing, and the loop of thread will be found gradually shortening as the tube sinks into the œsophagus. In that case the loop should be pulled upon, and the tube withdrawn. When quite satisfied that the tube is in the larynx, the operator removes the gag and waits a few minutes to allow the cough to remove the mucus and fragments of softened membrane. It is recommended that the gag should be then replaced, and the loop cut close to the mouth, and while the left index finger is passed down on the head of the tube to steady it, the thread should be drawn out, but in many cases it is better to leave the thread in for a short time, fastening it to one or other cheek by a small strip of plaster.

When the tube has to be extracted, the patient is placed in the same position as for introduction. The gag is inserted, and the left index finger is passed behind the epiglottis till it feels the opening in the head of the tube. The extractor, in the right hand, is introduced, and its point guided into the opening by the finger. By pressing on the lever in the handle the blades are dilated, thus holding the tube firmly while it is withdrawn.

Intubation is an easy and safe operation in the hands of an operator possessed of moderate dexterity and a thoroughly practical acquaintance with the parts dealt with, but to one not accustomed to put his finger in this part of the throat, the first attempt will often be attended with difficulty or failure.

As we have remarked in the paper already referred to, it is in a sense a tribute to the merit of intubation that the most successful results have hitherto been obtained by practitioners, not laryngeal specialists. With the gag in the mouth it is perfectly possible to see the glottis with the laryngoscope, especially with the aid of Dr. Bleyer's traction-hook, which exposes the epiglottis, and it is not only more easy and rational, but obviously far more safe, to introduce the tube by means of the eye than by the sense of touch, especially as by the introduction of the hand there is great risk of increased suffocation as well as of injury to the soft parts in a condition of inflammation or ulceration. Moreover, to learn the knack of introducing an instrument by sight requires no more practice than the guiding of it by the sole aid of the finger, and the same may be said as to its extraction.

After the tube has been placed in the larynx, and after the first effects of irritation have passed off, respiration will usually be carried on easily. It has occasionally happened that during the introduction false membranes have been detached and pushed down before the tube, thus causing suffocation. The accident is rare, and when it has happened immediate removal of the tube has almost invariably been followed by coughing up of the membrane. Should this not occur, tracheotomy should be done, and it is therefore well to have tracheotomy instruments ready at hand.

During the course of the treatment the tube is cleared of mucus by the ordinary efforts of respiration and cough. If it become clogged it is usually coughed up. There is, as a rule, no danger of suffocation in such cases for some hours, so that ample time is usually allowed to summon the physician or surgeon in charge. Sometimes the tube is coughed up independently of getting blocked. When the tube is very easily coughed up, it is an indication that the size used is too small.

It is usually ejected from the mouth, but it has occasionally been swallowed, and in all the recorded cases where this has happened (with one exception, when it was found *post-mortem* no further down than the stomach), it has been passed without difficulty *per rectum.* The tube must be extracted at any period of the treatment if there are symptoms of its being obstructed. Otherwise, most operators do not interfere with it. In the course of from four to six days the swelling and spasm will have so far diminished that the tube will be coughed up, and it will then probably be found that it is no longer required. If about the sixth day it be not coughed up, it should be removed with the extractor and need not again be introduced if the breathing is easy.

Some children after intubation swallow without difficulty both liquids and solids. In others, each attempt to swallow, more especially liquids, excites cough, owing to the entry of some portion into the air-passages. Semi-solid food is therefore preferable. It is, however, usually possible to overcome the difficulty of swallowing, even of liquids, by placing the child on its back in a horizontal position with its head hanging backwards, as described by Casselbury. In this position the child may suck from a bottle or be fed with a spoon. In some cases the child swallows as well or better lying on the abdomen with the head hanging forwards—that is, in the same position as that found to be convenient in cases of dysphagia due to tuberculous ulceration of the epiglottis.

CHAPTER XII.

HYGIENE AND PROPHYLAXIS OF DIPHTHERIA.

THE preventive measures to be observed with regard to diphtheria differ in no great respect from what would be required in the case of any other infectious or contagious disease.

They pertain not only to the patient and his surroundings, but also to the nurses and others in attendance during the attack, with a view to the prevention of the conveyance of the contagium from the sick-room to others. Secondly, to the disinfection of the sick-room, furniture, toys, clothing, &c., and to the correction of all sanitary defects which may be in any degree responsible for an outbreak, and lastly to systematic measures of prophylaxis in schools and school-houses.

As to the surroundings, every opportunity must be embraced of purifying the air of the sick-room and purging it of noxious exhalations; this purpose is best effected by securing to the patient an atmosphere well charged with oxygen. Every precaution must be taken against a further development of the poison as conveyed in the defæcations and eliminations of the tainted individual. All excretions should be treated with strong liquid disinfectants, and the W.-C. employed for their bestowal should not be used even by the immediate attendants,—in fact, in this respect every precaution should be observed as would be enforced were the case one of enteric fever.

Since disinfection of the atmosphere by chlorine, euchlorine, iodine, bromine, sulphurous acid, or any of the other more active but somewhat suffocative disinfectants is not generally feasible in the patient's room or immediate neighbourhood, the atmosphere

passing to and fro the doors and passages of the sick-room may be asepticised by sheets soaked in Burnett's fluid, sanitas, eucalyptus, and similar solutions.

A "Sanitas" kettle may be conveniently placed outside the room over a Bunsen gas burner, so that when the door is opened the air comes in not only warm and moist, but impregnated with oxidising constituents. Sprays of Condy's fluid, Sanitas, &c., by means of hand-ball or steam atomisers may also be employed in the room.

Nothing should be allowed to go from the sick-room unless previously treated with disinfectants. All utensils—plates, cups, forks, spoons, &c.—used by the patient must be immediately disinfected by being washed in some germicide solution, such as perchloride or biniodide of mercury. In cases where the water supply is suspected as a source of infection, all water used for the patient and household should have been previously boiled; the same precaution should be observed with regard to milk, whether or not its purity be under suspicion.

Old linen rags are preferable to the ordinary pocket-handkerchiefs, as they can be burnt after use; and every dressing, poultice, &c., should be immediately committed to the fire, which for purposes of preparation of food, &c., should always be kept burning in an adjoining chamber if the season of the year does not require it in the sick-room. Articles of clothing, bed-linen, &c., should be placed in a suitable receptacle containing a solution of 1 in 2000 perchloride of mercury, or 1 in 4000 biniodide of mercury, before being removed from the chamber occupied by the patient.

The nurses and attendants should wear blouses which can be removed on their leaving the patient, and the medical attendant would also do well to wear a similar protective dress before entering the patient's room. Scrupulous attention must be observed in well washing the hands, brushing the finger-nails, &c., with disinfectant solutions after every visit to the patient, and the physician would be acting wisely in refraining from visiting any young children for a few hours after attending a case

of diphtheria, and even then only after a complete change of clothing.

Sufficient insistance has been made on the all-important confirmation by bacteriological examination of the clinical diagnosis of diphtheria directly a case comes under observation. It is also equally important that by the same means the thorough recovery of each individual attacked should be accuratcly determined. We have already remarked that the aerial communication of diphtheria from bed to bed in hospitals is in all probability of rarc occurrence; but we are not at all so sure that there is equal immunity in regard to the infectiousness of such septie conveyance as may be due to the association of diphtheria bacillus with coccal organisms; and Moizard has urged that in hospitals where diphtheria is treated, every patient suffering from broncho-pneumonia, or other complication of a septic nature, should be isolated as a routine measure.

This course of action might, however, be somewhat difficult to carry out in ordinary practice, and its mere suggestion may perhaps be regarded as an undue refinement of prophylaxis; but it is by no means as fanciful as may at first sight appear. For we have noted in quite a considerable number of our cases in which the first bacteriological examination has proved the diphtheria bacillus to have been associated only with single cocci or diplococci, that a second examination similarly conducted in the convalescent stage has—while declaring the bacillus diphtheriæ to be absent—noted the appearance of other organisms of greater importance than those originally present, especially streptococci.

These bacteriological examinations of convalescent patients are of the morc importance, because in diphtheria no clinical criteria exist of complete recovery similar to those evident in scarlet fever, smallpox, chicken-pox, whooping cough, measles, and the like.

The length of period that the bacilli of diphtheria may remain in the throat in a state of virulence varies very considerably.

Loeffler and Park maintained it in an active state for seven months on blood-serum. Roux and Yersin found the bacillus in

dried shreds of membrane in a condition of virulence after twenty weeks; and Morell Mackenzie has related several cases, which occurred in pre-bacteriological times, proving that the appearance of sporadic cases of diphtheria could only be accounted for by an equal or even longer period of vitality of the bacillus.

The following statistics made by Park and Beebe are of interest:—

Out of a total number of 605 cases of diphtheria which recovered, these observers found that in 304 the bacillus disappeared within three days after the disappearance of the exudate; in 176 cases the bacilli remained for 7 days; in 64 cases, for 12 days; in 36 cases, for 15 days; in 12 cases, for 21 days; in 4 cases, for 28 days; in 4 cases, for 35 days; and in 2 cases, for 63 days after the disappearance of the membrane. In all of these cases the specific microbes, although growing gradually less numerous and becoming more admixed with cocci, were still virulent, and generally to the date of their final disappearance. In the foregoing pages we have reported how bacilli in a state of attenuation were found to be present on a wound after tonsillotomy, three months after the patient's discharge from the hospital (*Case* 4).

We have also followed the history of another case in which diphtheria bacilli in full activity and virulence were found 80 days after the patient's throat was clear of all exudation. And a third case has been recorded (*Case* 13), in which the patient engaged officially in the diphtheria wards of an Infectious Fever Hospital, had four attacks of the disease in a period of three years. Nevertheless, examination on the 24th day after the fourth attack failed to detect the presence of any bacilli of diphtheria in the patient's throat.

And yet again, we have mentioned an instance of croup (page 183) in which there was never any but the slightest sign of exudation—and that only in the larynx. Bacilli, however, were found in the secretion from the throat upwards of a month after intubation had been performed, the only sequelæ being slight loss of reflexes.

In view of the existence of these elements of uncertainty, it would appear to be impossible to exercise too much caution in respect of definite confirmation of complete recovery.

The throat of every patient recovering from diphtheria should be syringed, and treated with antiseptic gargles and solutions. Bacteriological examinations should be regularly made once a week, until they fail to detect the presence of the specific bacillus. Moreover, in regard to what has been said of the presence of the bacilli in the throats of those attending on diphtheria patients, the same precautionary measures of gargling and bacteriological examination against the conveyance of infeetion to susceptible persons should be strictly enforced; for we have knowledge of the fact of diphtheria occurring three times in the daughter of a medical superintendent of a fever hospital (the lady in question never having visited the wards). Her first attack came when she was three years of age and the last when she was nineteen.

In the event of fatal termination to a case, it is most advisable that relatives not previously in attendance should abstain from even visiting the siek-room, mueh less run risk of contagion by kissing the deceased. This precaution is to be specially observed with regard to young children.

Doctors and nurses each time after being in close contact with a patient might observe a hint which we have adopted from the practice of a sanitary engineer, who, whenever he was obliged to inhale any unpleasant effluvium, blew his nose freely, gathered his saliva, and expectorated.

A recent editorial article in the *Lancet* has well said that "the prevention of the spread of diphtheria through the agency of schools is certainly one of the most difficult duties which devolve upon the medical officer of health. On the one hand he is prompted to school closure or the exclusion from school of children from infected localities or houses; and on the other, he is anxious, as far as possible, not to interfere unduly with the educational work of the institution and the prospect of the Government grant."

We have already given our reasons for the opinion that the mode in which diphtheria is disseminated by what has come to be called "school influence" has been generally misunderstood, and have endeavoured to show that the disease does not originate in the school, but that it is usually introduced from the home, to be afterwards very likely transmitted and disseminated to other homes from the school.

Many medical officers of health are commencing to realise this fact, and several have recently instituted a systematised examination of the throats of all children on the re-assembling of schools, relegating those who appear at all affected to their homes for treatment and exclusion; and for the inspection and remedy of any sanitary defects apparent therein. This last is essential in any case, and whenever operative measures, such as the removal of tonsils, faucial or pharyngeal, are indicated, it is desirable to insure that there is no diphtheria or other infectious disease existing in other members of the same household.

Where these precautionary measures of examination have been systematically adopted a remarkable diminution of diphtheria and other infectious diseases has been noticed in districts where they have long previously been endemic, and as a consequence school closure and interference with regular education is becoming less frequent.

But we would urge that something more should be done. We have seen that a considerable proportion of outbreaks of diphtheria has been preceded by attacks, not only of enteric and scarlet fever, but of other non-notifiable diseases, such as measles and simple sore throat. To these might be added chicken-pox, German measles, and whooping-cough, which are known to increase the gravity of an attack of diphtheria to such an extent, indeed, as to merit statistical notice in the Annual Reports of the Asylums' Board for the current year.

Parish councils, school boards, and other ruling bodies under the growing influence of extended local government should recognise their responsibility in the matter of other diseases, than those

included under the Notification Act, capable of being fostered in school buildings and others where many persons are congregated, and should make arrangements for the periodical inspection of all schools by responsible medical practitioners, preferably the medical officer of health.

Indeed, such an officer ought to be attached to all these bodies, and we are convinced, from the present high qualifications required from public health officers, that their presence on all committees relating to the erection of new buildings and the maintenance of good sanitation would be attended with results of far-reaching value and of true economy.

Throat examination.—For this purpose it is necessary to have a metal tongue depressor, a laryngeal mirror, and a nasal speculum; a separate tongue cloth should be used for each child and immediately burnt. The attendant should, after each examination, disinfect all the instruments in some strong antiseptic solution, at high temperature, of either lysol, cresol, or biniodide of mercury.

In all cases in which the patients have contracted the habit of mouth-breathing, measures operative or otherwise should be adopted to reduce to a minimum the chances of recurrence of an attack of diphtheria, and the same should be adopted in other members of the family, and, indeed, of all children who are thus possessed in a high degree of receptivity to diphtheria and associated infectious diseases of the throat.

Preventive surgical treatment.—This is not the place to describe methods of operation, but a hint or two may be here given as to the removal of the tonsils, both faucial and pharyngeal.

(1.) When the faucial tonsils are unequally enlarged, it is well to remove both, for, as in the case of tonsillitis, the inflammation having been reduced on one side is very apt to pass to the other, so if one tonsil only be removed the other is very liable to become hypertrophied.

(2.) In all children under puberty, and in some adults in whom

the tonsils are large, there is almost always similar overgrowth of the pharyngeal tonsil. It is not necessary to put a child to the somewhat terrifying procedure of exploration with the finger behind the soft palate for diagnostic purposes prior to operation, but the vault should always be examined and, if necessary, cleared as a logical complement of a faucial tonsillotomy.

(3.) Cases undoubtedly exist in which the pharyngeal tonsil is enlarged without overgrowth of the faucial. In these cases there is generally some thickening of the faucial pillars, indicating chronic inflammation. By closing first one and then the other of the nostrils by the finger and causing the patient to breathe on to the hand of the examiner, a good idea of the amount of obstruction to nasal respiration can be obtained. In cases where there is reflex laryngeal cough, nasal catarrh, and liability to head cold, &c., one may with certainty predicate adenoid vegetations, and this even in cases in which there may be also evidences of a specific dyscrasia.

(4.) In almost all cases of nasal and faucial stenosis there is paresis of the soft palate with relaxation of the uvula, but we make it a rule, to which there is hardly an exception, not to remove any portion of the uvula of a child under the age of puberty at the same time that we perform faucial tonsillotomy or naso-pharyngeal curetting; having found in almost all cases that muscular tone will quickly be regained when once free nasal respiration is restored.

(5.) In like manner there is some turgidity of the turbinal bodies in cases of nasal stenosis, which has been called hypertrophic rhinitis, but this term is clearly a misnomer when applied to young children: for one cannot talk of an overgrowth of tissues which are not fully developed until puberty, as is the case with the turbinals.

On this account we rarely treat the turbinal congestion by any active means, finding that it also almost always disappears so soon as congestion is relieved by removal of adenoids and the re-establishment of nasal respiration.

(6.) We do not advise the use of the nasal syringe in the chronic catarrhs of young children, since, as Bosworth says, the parts are already "waterlogged" by a hyper-secretion of moisture. In these circumstances nasal douches are but too likely to induce a life-long nasal catarrh. In any case we never syringe more than two ounces of a solution into each nostril on any one occasion, whether the patient be child or adult.

Disinfection of the sick-room after the termination of a case of diphtheria.—Disinfection in private residences is generally carried out by officials in the employ of the sanitary authorities of the particular district in which the patient resides.

All bedding, pillows, blankets, mattresses, carpets, curtains, &c., are effectually disinfected by treatment with super-heated steam, for which purpose they are sent to the nearest disinfecting station. The proper disinfection of the sick-room, however, offers more difficulty.

Having knowledge of many instances in which the official course of disinfection has proved to be inadequate, a brief outline of the necessary steps which should be taken to speedily and effectively disinfect a room or rooms in which diphtheria cases have been treated will not be considered superfluous.

Among the many methods of disinfection the burning of sulphur with the production of sulphurous acid is perhaps the most common and the most efficacious when properly carried out.

It is necessary for perfect disinfection that the room should be as far as possible hermetically closed; the windows tightly shut, the register of the fire place pulled down, and every outlet, chink, and crevice blocked up.

One pound of sulphur—preferably in the convenient form now supplied under the name of "sulphur candles"—should be provided for every 1000 cubic feet of air space to be disinfected. It is particularly to be noted that to produce the most effectual results from sulphur combustion an adequate supply of moisture must be present. For this purpose, the vessel in which the sulphur is burnt may with great advantage be placed in a large flat pan

filled with steaming water; and similar pans of water should be placed in other parts of the room which is to be disinfected. The combustion of the sulphur results in the production of the dioxide; this gas in the presence of aqueous vapour becomes sulphurous and subsequently sulphuric acid. It is on these chemical changes that the powerful disinfectant action of sulphur in a state of combustion depends.

Other oxidising agents, such as ozone, produced by the action of sulphuric acid on permanganate of potash; nascent chlorine, generated by the action of sulphuric acid on a mixture of common salt (chloride of sodium), and dioxide of manganese, or by hydrochloric acid on bleaching powder (chloride of lime), may be employed for disinfecting purposes.

The room should be kept closed for eight to twelve hours after any of these procedures. At the expiration of that period all the windows and doors must be opened, and kept open for twenty-four hours.

Further, it is necessary for complete success that the wall papers should be stripped; the ceiling redistempered or painted; the floor, woodwork, and indeed the whole room thoroughly washed with soap and water, followed by a further cleansing with either a solution of 1 in 2000 of perchloride of mercury, or of 1 in 20 of carbolic acid. Unless some such means are adopted after a case of diphtheria occurring in a private residence, prophylaxis against further infection cannot be considered to have been pursued to complete efficiency.

Finally all defects in sanitary surroundings which might be reasonably held to be responsible for an illness or outbreak should be rigorously searched for, and when found should be immediately and thoroughly corrected.

CHAPTER XIII.

FORMULÆ FOR REMEDIES IN DIPHTHERIA.

THE following short list of prescriptions of the remedies useful in the treatment of diphtheria and its associates is for the most part limited to those mentioned in the text, and is by no means held to be in any degree exhaustive. To prolong it would, however, only lead to confusion.

The dosage of the mixtures is—unless otherwise stated—arranged, as in the Pharmacopœia of The Central London Throat, Nose, and Ear Hospital, on the plan of prescribing the amount for an adult dose as half-an-ounce. The quantity to be administered to patients of varying ages is, therefore, easily calculated, and may be indicated on the prescription by ordering the dose as 1, 2, 3, or 4 teaspoonsful, as required.

In some instances it may be desirable to dilute these doses with an equal quantity of water. The interval between each separate dose should be from four to six hours.

In the case of a disease such as diphtheria, which for the most part attacks young children, some variation in the doses will be required to be made for differences of even a year or two in the patients' ages, and also according to the personal equation of vital and assimilative power in each individual instance.

To these prescriptions for medicinal remedies there will be added some formulæ for preparing staining solutions for microscopical examinations, and a few directions as to beverages and articles of diet, which may be found useful by the young practitioner.

It will be observed that there are no prescriptions given for

Gargles, but all the Lotions can be used for that purpose. Considering the tender age of most of the subjects of diphtheria gargling of any kind is almost impossible, and even with those old enough to understand, as pointed out in our chapter on treatment, the procedure is liable, by putting the faucial and palatal muscles into undue and irregular action, to favour the occurrence and severity of palatal paresis. It is, therefore, better that the lotions should be used as mouth washes, or as irrigations with the special syringe recommended (page 171).

When gargles are used the method of Von Tröeltsch should be pursued. This consists in taking the necessary quantity into the mouth, closing the nose with finger and thumb, throwing back the head and making repeatedly the half act of swallowing; the procedure requires, however, some amount of intelligence to perform efficiently, otherwise the accident may occur of swallowing the solution, or of letting it into the wind-pipe. It is for this reason we do not recommend gargles to be composed of ingredients of a character likely to prove at all harmful to the general system.

No attempt has been made to render any of these prescriptions "elegant," the agreeableness of a medium being a question which may well be left to the experience of each practitioner. There is, however, one exception.

We have expressed a preference for mouth washes composed of mercuric biniodide over those of the perchloride for reasons of efficacy; probably from their lessened tendency to coagulate albumen they are also more palatable; nevertheless, the mineral flavour is to many a drawback to the use of either. This we have found may be greatly diminished, if not entirely overcome, by their administration in a medium of strong Elder flower water, and a form for such a prescription is therefore given.

Mixtures.

(1) Mistura Sodii Salicylatis Composita.

℞ Salicylate of sodium, . .	8 grs.
Chlorate of sodium, . .	6 ,,
Spirit of chloroform, . .	10 m.
Decoction of cinchona, . .	to ½ fluid ounce.
	Mix.

(2) Mistura Ferri perchloridi.

℞ Solution of perchloride of iron, .	20 m.
Chlorate of sodium, ...	8 grs.
Glycerine, ...	½ dr.
Chloroform water, ...	to ½ fl. oz.
	Mix.

(3) Mistura Hydrargyri Biniodidi.

℞ Solution of perchloride of mercury (P. B.),	1 dr.
Iodide of sodium or potassium, . .	4 grs.
Peppermint water, ...	to ½ fl. oz.
	Mix.

Adult dose, ½ oz. For children, 1 dr.

(4) Mistura Ferri cum Strychninâ.

℞ The same mixture as No. 2, with the addition of the solution of strychnia (P. B.) 3 m. to 5 m. for each dose. The smaller amount can be taken by children up to five or seven years old.

(5) Mistura Diuretica. (Kidney Mixture.)

℞ Solution of perchloride of iron, .	20 m.
Solution of acetate of ammonium, .	80 m.
Chloroform water, ...	to ½ fl. oz.
	Mix.

(6) Mistura Antispasmodica. (Croup Mixture.)

℞	Bicarbonate of soda, ...	15 grs.
	Wine of ipecacuanha, . . .	5 m.
	Syrup of chloral	5 m.
	Water, ...	to 2 drs.
		Mix.

This is the dose for a child five years old or above. For children under five, the dose may require to be modified to half, or less than half, the quantity.

(7) Potus Diureticus.

℞ Solution of the perchloride of iron is added to lemonade or barley water (sweetened), in the proportion of 5 drops of the iron solution to every ounce of the drink. Children may take nearly a quart of this in 24 hours—representing over 3 fluid drachms of the iron—with no other than a beneficial effect.

(8) Confectio Potassii Chloratis.

℞	Chlorate of potassium, ...	10 grs.
	Honey, ...	1 oz.
		Mix.

One teaspoonful every 2 or 3 hours, for young children.

TOPICAL REMEDIES.

(9) Pigmentum Acidi Lactici.

℞ Lactic acid (P. B.)

For application once or twice a day by the medical practitioner.

(10) Pigmentum Acidi Lactici diluti.

℞	Lactic acid (P. B.), ...	1 part.
	Distilled water, ...	3 parts.
		Mix.

For application by the nurse or attendant every 3 or 4 hours.

N.B.—This may be employed as a laryngeal or nasal application by the medical practitioner, either by means of a brush or as a spray to the affected parts.

(11) Pigmentum Ferri perchloridi.

℞ Perchloride of iron, . . .	1 part.
Distilled water, ...	4 parts.
	Dissolve.

For application by brush or swab.

(12) Pigmentum Menthol.

℞ Menthol, ...	1 part.
Oil of sweet almonds, . . .	5 parts.
	Dissolve.

For application along the floor of the nostrils by brush or cotton wool swab.

(13) Nebula Menthol.

℞ Menthol, ...	10 grs.
Oil of sweet almonds, . . .	to 1 fl. oz.

To be employed by spray to nose, throat, or larynx.

(14) Lotio Alkalina Antiseptica. (Dobell.)

℞ Borax, ...	2 drs.
Bicarbonate of sodium, . . .	2 drs.
Glycerine of carbolic acid, . .	4 drs.
Distilled water, . . .	to 10 oz.
	Mix and dissolve.

This excellent cleansing and antiseptic solution is prescribed in double strength, and should be diluted with an equal quantity of hot water to bring it to the proper strength and temperature. It may be employed by the syringe or by means of a Lefferts' coarse spray.

(15) Lotio Alkalina.

℞ Chlorate of potassium, . . .	$\frac{1}{2}$ oz.
Bicarbonate of sodium, . . .	$\frac{1}{2}$ „
Borax, ...	$\frac{1}{2}$ „
White sugar (in powder), . . .	1 „
	Mix.

A teaspoonful dissolved in 5 or 10 ounces of water at 95° F. to be used as a gargle or mouth wash with irrigator, or as lotion to the nose with the nasal syringe.

(16) Lotio Hydrargyri Perchloridi.

℞ Perchloride of mercury, . . .	$\frac{1}{4}$ gr.
Water, ...	1 fl. oz.
	Dissolve.

(This solution is equal to 1 in 2000.)

For application by swab or irrigating syringe.

(17) Lotio Hydrargyri Biniodidi.

℞ Red iodide of mercury, . . .	$\frac{1}{4}$ gr.
Iodide of sodium, ...	$\frac{1}{4}$ gr.
Water, ...	1 fl. oz.
	Dissolve.

(This solution is equal to 1 in 2000 of the biniodide.)

To be applied as above.

(17 bis) Lotio Hydrargyri Biniodidi Odorata.

℞ Red iodide of mercury, . . .	2 grs.
Iodide of sodium, ...	4 grs.
Elder flower water (concentrated 1-3),	℥ viii.

To be used as a gargle, mouth wash, or for oral irrigation.

One part of this lotion to three of water makes a solution of the strength of 1 in 6000.

(18) Lotio Chlori.

℞ Chlorate of potash, ...	30 grs.
Hydrochloric acid pure, . . .	30 m.
Water, ...	to 10 oz.

Dissolve the chlorate of potash in the water, and gradually add the acid. This lotion should be kept in a stoppered bottle, and should be made fresh every day.

(19) Lotio Acidi Carbolici.

℞ Glycerine of carbolic acid (P. B.). For use, mix in the proportion of a teaspoonful to half-a-tumbler of tepid water.

Recommended as a mouth wash or gargle in cases of pseudo-diphtheria, especially where there is much muco-salivary secretions (as in tonsillitis).

(20) Lotio Acidi Borici.

℞ Boracic acid, ...	1 part.
Water at temperature of 100° F., .	25 parts.
	Dissolve.

For oral irrigation and also for syringing the external auditory meatus in cases of suppurative otitis.

(21) Loeffler's Solution.

℞ Alcohol, ...	64 parts.
Toluol, ...	36 parts.
Creolin or metacresol, . . .	1 or 3 parts.
Menthol, ...	10 parts.
	Mix.

For local application by brush or swab in diphtheria, but probably better in pseudo-diphtheria.

22. Unguentum Antisepticum.

℞ Hydrochlorate of cocaine, ...	30 grs.
Boracic acid, } Salicylate of sodium, } . .	of each 40 grs.
Creolin, ...	2 fl. drs.
Eucalyptus oil, ...	10 m.
Vaseline, ...	to 1 oz.
	Mix.

For application to the nostrils.

(23) Vapor Pini Sylvestris. (C. T. H.)

℞ Firwood oil, ...	40 m.
Light carbonate of magnesium, . .	20 grs.
Water, ...	to 1 oz.
	Mix.

One fluid drachm in a pint of water at 140° F. for each inhalation, either by special inhaler or in steam-kettle.

(24) Vapor Benzoini cum Chloroformo.

℞ Compound tincture of benzoin, . .	1 fl. oz.
Chloroform, ...	8 m.
	Mix.

A teaspoonful in a pint of hot water at 140° to 150° F. for each inhalation, or as in the foregoing.

Staining Solutions for Microscopic Preparations.

(25) Loeffler's Solution. (Squire.)

℞ Concentrated alcoholic solution of methylene blue, ...	30 parts.
Solution of caustic potash (1 in 10,000 of water), ...	100 parts.
	Mix.

Place coverglasses in this solution for three to five minutes, wash, dehydrate, clear, and mount in balsam.

(26) Roux's Double Stain.

℞ Dahlia or gentian violet, . . .	0·5 grm.
Methyl green, ...	0·5 grm.
Distilled water, ...	200 c. c.

Mix and filter before use.

Sections are placed in this stain for twelve hours, then washed, dehydrated, cleared, and mounted.

(27) **Gram's Method.** (Squire.)

Place section in the following solution :—

Aniline water, ...	100 parts.
Concentrated solution of gentian violet,	11 ,,
Absolute alcohol, ...	10 ,,

for one to three minutes. Rinse in absolute alcohol, and transfer to Gram's solution :—

Iodine, ...	1 part.
Iodide of potash, ...	2 ,,
Distilled water, ...	300 ,,

until they acquire a brown colour; this takes place in about one to three minutes. The sections are then washed in 90 per cent. alcohol, until they are a pale yellow colour, dehydrated, cleared and mounted in balsam.

Articles of Diet.

Beef Tea.—Take one pound of beef without fat or bone, mince and bruise the meat with pestle and mortar; place it in a jar containing a pint of cold water; set the jar in a sauce-pan of hot water and allow to simmer four hours.

N.B.—This, as well as other meat, broths, and milk, may require to be peptonised.

The following directions are given by Sir William Roberts for the preparation of peptonised nutriment :—

Peptonised Beef Tea.—A pound of finely-minced lean beef is mixed with a pint of water, and ten grains of bicarbonate of sodium added. The mixture is then simmered for an hour and a half in a covered saucepan. The resulting beef-tea is decanted off into a covered jug. The undissolved beef residue is then beaten up with a spoon into a paste, and added to the beef-tea in the covered jug. When the mixture has cooled down to about

140° F. (or when it is cool enough to be tolerated in the mouth), a tablespoonful of *liquor pancreaticus* (Benger) is added, and the whole well stirred together. The covered jug is then kept warm for two hours under a "cosey" and agitated occasionally. At the end of this time the contents of the jug are boiled briskly for two or three minutes and finally strained. When seasoned with salt it is scarcely distinguishable from ordinary beef-tea.

Peptonised Milk.—A pint of milk is diluted with a quarter of a pint of water, and heated to 140° F. Two teaspoonsful of *liquor pancreaticus* (Benger), and ten grains of bicarbonate of sodium are then added to the warm milk. The mixture is poured into a covered jug, which is placed in a warm situation for one or one and a half hours, and then boiled for two or three minutes. It can then be used like fresh milk.

Lemonade.—Pare the rind of three lemons as thin as possible, add one quart of boiling water and a quarter of an ounce of isinglass. Let them stand till next day covered, then squeeze the juice of eight lemons upon half a pound of lump sugar; when the sugar is dissolved, pour the lemon and water upon it, mix all well together, strain it, and it is ready for use.

Barley Water.—To a tablespoonful of pearl barley in cold water add two or three lumps of sugar, the rind of one lemon, and the juice of half a lemon. On these pour a quart of boiling water, and let it stand in lidded vessel and covered with baize or "cosey" for seven or eight hours; strain it. The barley should never be used a second time. Half an ounce of isinglass may be boiled in the water.

APPENDIX.

THE SERUM TREATMENT OF DIPHTHERIA.

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PREFATORY NOTE.

The reasons for considering this subject as an appendix hardly need detailed explanation.

Serum treatment is said to be still on its trial, and on this account as well as in view of the facts to be recorded, we do not feel justified in giving it a position as an integral portion of our therapeutic resource alongside of the older, well tried, and well established methods of the classical treatment of diphtheria.

We must all cordially agree with Professor Virchow's opinion that the brute force of the figures which have been displayed as representing a marvellous diminution in mortality not only in one, but in many centres of observation, cannot but compel all humane physicians to give the so-called antitoxin treatment an impartial trial.

On the other hand, many—and we are of that number—must sympathise with the modified ardour of Professor Bergmann, who, reported as still suffering from the scars left by the Tuberculin conflagration, has deprecated acceptance of the serum treatment of diphtheria with that almost blind enthusiasm which was accorded to Koch's remedy on the high reputation of its author.

We well remember the caution that Professor Syme used to give his students, that it was easy to discover any sequence of symptom or result which we might decide to find. In other words, that the adage of the wish being father to the thought is of special aptitude in medical diagnosis and therapeutics. And this is particularly true of all those remedies that come to us from the microbo-biological laboratory.

If we were to judge solely by the mere returns of diminished mortality so prodigally supplied in current literature, the reputation of the serum treatment ought to be firmly established; but with all deference we suggest that these returns may be divided into two classes: the first, consisting of several short series of cases from observers of limited ex-

perience, which illustrate nothing, since there has been no distinction made between the mild cases, which, as we all know, have a natural tendency to cure, whatever be the treatment, and the graver class, which must constitute the crucial test. The other, and larger class, is represented almost uniformly by the results in hospitals in which the former mortality has been abnormally high. Thus, the return made by Roux of a mortality of 51·7 per cent., reduced by serum treatment to 24·5 per cent., gives a ratio hardly better than that attained for some years past, in more than one Metropolitan Fever Hospital, by the old methods. Moreover, as conceded by Moizard, physician to the Trousseau Hospital in Paris, the diminished mortality at that institution (and at many others) may to a large extent be accounted for by the highly necessary hygienic improvements which have been carried out concurrently with the trial of this new remedy.

It appears probable that in Serum therapy, as in the case of Antiseptic surgery, the scrupulous cleanliness which is indispensable to it may, quite irrespective of the medicament employed, be a not unimportant factor in the improvement of results.

The subject of serum treatment will be considered by us with all the fulness of detail demanded by the claims advanced on its behalf, and with every direction for its administration as will enable it to be pursued by those desirous of testing its efficiency. No attempt will be made to explain away figures reported by other observers. Indeed, they will but rarely be quoted, for our own conclusions will be illustrated by a comparison of results in a series of 100 cases treated by the serum, with another series of 100 cases treated without serum, at a corresponding period of the previous year.

The following is one of many circumstances of a misleading tendency which led us to take this step of separate and independent observation and comparison. An unofficial report had been published in the *Lancet* and *British Medical Journal* of results in the Isolation Hospitals of London, after hardly more than three weeks' official trial of the remedy,—cases being included that had only been admitted one or two days previously. The author of this report thus ascribed a percentage mortality of 4·6 per cent. on 43 cases at the hospital where we have been watching the treatment—"the lowest mortality on record." Within two days of publication of these figures this mortality became over 8·0 per cent.; three weeks later it was 19 per cent.; and as the figures we have collected show, it was finally, at the end of four months, 27 per cent., practically the same mortality as had obtained for the two previous years by the older methods in nearly 2500 cases. Unfortunately, the first percentage of 4·6 has been largely circulated, and is still accepted and quoted as a record.

Again, we personally having stated that out of five cases we had already lost two, were credited in prints widely distributed, with three recoveries out of five cases; whereas out of our first eight cases only two recovered.

The **history** of this method of treating infectious diseases by the injection of some substance which is capable of antagonising its specific poisonous effect is, albeit of some interest, but a short one.

The application of the principle cannot be said to have resulted from any one brilliant discovery, but may rather be described as the gradual development and outcome of the labours of many individuals.

The scientific investigation of the subject dates from 1860, when PASTEUR made the first announcement of his classical researches upon *ferments*. Thence he was led to study the mode of action of bacteria, and his labours in this direction prompted METCHNIKOFF and others to study human reaction to the presence of these pathological micro-organisms. METCHNIKOFF'S epoch-making statement of the part played by phagocytes in the body is known to all; but it is only fair to say that his conclusions have been vigorously opposed, and albeit they have been deemed reasonable by many competent critics, they must not yet be accepted as absolutely proven.

The therapeutic method itself may also be said to date from PASTEUR, with his discovery, in 1880, that a mild attack of *fowl cholera* can be induced in chickens by inoculating them with an attenuated virus, that is to say, with a culture of the pathogenic microbes of the disease, the virulence of which has been reduced by cultivating them in an unsuitable medium, so as to impede attainment of their full virulence.

This mild attack rendered the chickens immune to fowl cholera, and the next advance was made by the same investigator when he applied this discovery to *anthrax*.

In some respects *vaccination* for smallpox may be said to have foreshadowed these and other similar results; the difference, however, between them and modern serum therapy consists in the fact that the former, having been pursued on a much less scientific basis, cannot be looked upon as having done more than indicate the practicability of combating disease by methods of inoculation.

In 1886 Salmon and Smith showed that the principle discovered by Pasteur was applicable to *hog cholera.* Roux about the same time demonstrated that sterilised cultures of anthrax bacilli induced *charbon* in the subjects inoculated. In all of these cases it was found that the mild attack excited by inoculation with the attenuated virus rendered the animals immune to further attacks of the same disease, not only in attenuated but in virulent form.

A further advance was made when Nuttal, Behring, Buchner, Tizzoni, Cattani, and others, showed that recently drawn blood had in certain cases an undoubtedly germicidal power. The same properties were also evinced by aqueous humour, ascitic fluid, and lymph drawn from the dorsal lymph-sinus of the frog.

It soon became evident that the blood of different animals exercised, as it were, a specific effect with regard to definite microbes. Thus Behring discovered that blood taken from the rat or the frog was especially efficacious against anthrax bacilli, those animals being peculiarly refractory to the onslaughts of these organisms. It was further demonstrated, after a short time, that the germicidal power of the blood was only effectual within certain limits, and that a definite quantity of it was able to destroy only a correspondingly definite number of bacilli, so that its action was practically that of a neutralising body. Buchner ascribed this germicidal power to an albuminoid substance contained by these fluids.

In December 1890 Behring and Kitasato made the surprising announcement that if an animal is immunised against *tetanus* or *diphtheria*, its serum, injected in sufficient quantity into another animal, was able not only to immunise against an attack, but to cure one.

Here are the precise terms in which these two observers published their discovery:—

"Our researches on diphtheria (Behring) and on tetanus (Kitasato) have led us to the question of immunity and cure of these two diseases, and we have succeeded in curing infected animals and in immunising healthy animals, so that they have become incapable of contracting diphtheria or tetanus."

After the researches of BEHRING, it is only fair to mention those of ARONSON, who, with equal perseverance, succeeded in immunising animals against diphtheria.

HANKIN, in 1891, succeeded in isolating from the spleen and blood of rats a globulin possessed of germicidal powers, which, in his opinion, constituted the antitoxic or germicidal substance.

In the following year BRIEGER, KITASATO, and WASSERMAN cultivated tetanus bacilli in bouillon, prepared from the thymus of the calf, with the result that the bacilli became non-virulent, and did not form spores. Mice and rabbits, having been inoculated with this bouillon, became immune to attacks of tetanus on subsequent introduction of virulent cultures of the bacillus; and further, blood serum from an immune animal, when injected into a susceptible animal, conferred immunity upon it. Similar results were also obtained with several other pathogenic bacteria—as, for instance, with the bacilli of *typhoid*, *cholera*, and *diphtheria*.

Soon after this, OGATA and JASHURA discovered that when bacilli, previously attenuated by being cultivated in the blood of naturally immune animals, are injected into susceptible animals, they result in a mild attack, which confers subsequent immunity.

ARLOING has further shown that the reverse is also true—that is to say, that animals which are naturally immune to anthrax can be rendered susceptible to it if certain substances are mixed with the injection; and LEO has claimed that white mice, which are naturally immune to glanders bacilli, can be made susceptible by feeding them for some time before they are inoculated with phloridzin. This statement, however, needs confirmation.

Thus the last link in the chain was forged, and from this time on it was only necessary to apply the discoveries that had been made.

In this field, the work of BEHRING has been most productive.

The next problem that presented itself was, How can artificially acquired immunity be conveyed from animals to human beings who have acquired the disease? The supposition that diphtheria is a malady localised to the throat, for a long time stood in the

way of discovering a cure on these lines; and it was not until it was recognised that diphtheria, albeit of local origin, is a systemic disease, that any advance became possible.

It will be well, at this point, to take a general brief review of the treatment of infectious diseases by the introduction into the body of the serum of artificially immunised animals.

At the International Congress of Hygiene and Demography, which was held in London in 1891, HANKIN pointed out that the bactericidal action of the serum of immune animals is due to the action of certain defensive proteids, and that, whilst some of these act by killing the microbes, others destroy or neutralise the microbic products.

At the same meeting KITASATO again mentioned his discovery in conjunction with BEHRING—that the injection of the blood of rabbits which had been rendered immune to tetanus not only renders mice refractory to the affection, but also cures them of the disease when it is already in progress.

SIDNEY MARTIN (1891), in a special report to the Local Government Board, further demonstrated the nature of these microbic products as regards diphtheria. Then in 1892 KLEMPERER stated that the discoveries with regard to diphtheria are also applicable to other infectious diseases, and in March 1893 KLEMENSIEWICZ and ESCHERICH rendered guinea-pigs immune to inoculation with diphtheria by a preliminary inoculation with the blood serum of patients recovering from the malady. Closely following on this, BEHRING and KOSSEL recorded thirty cases of diphtheria in the human subject which had been beneficially treated with immunised serum. In this experience they were supported by HEUBNER of Leipzig.

The culminating point of enthusiasm was reached by ROUX in his brilliant paper at the Congress of Hygiene and Demography, which was held at Budapest in 1894. He announced himself as enabled to confirm, by experiments in the Pasteur Institute, all that had been claimed by BEHRING and other previous workers. He recorded a large number of cases in

which the treatment had been adopted on the human subject, and by comparative statistics, enforced the attention of the whole medical world to a consideration of its claims.

In concluding our brief historical review of this fascinating subject, we may mention that Roux in this address, advanced that "the question of preventive and therapeutic serums was born with the experiments of Maurice Raynaud on the blood of heifers inoculated for cow-pox; and with those of Richet and Hericourt, on the serum of dogs and rabbits vaccinated against septicæmia (1888)."

Lastly, it may be recorded, C. Fraenkel, Babes, and Ferrein, have each made claims to priority in these discoveries which can only receive here the recognition of mention.

Theory of Immunisation.—To render an animal immune to the diphtheria toxine, it is held sufficient to accustom it slowly to the action of that toxine. The serum of the animal thus immunised is believed to then become a vaccine, possessing qualities not only preventive, but arrestive and curative.

It is declared that this mode of protection is evidently immensely superior to the direct immunisation obtained by injecting the toxine itself, which is, moreover, too slow to be of use in the treatment of an acute disease.

In addition, the action of the serum—this second hand product—is claimed to be *immediate,* with the further property of conferring a *temporary* immunity.

Preparation of the remedy.—We are now in a position to study the processes employed to obtain the toxine, and to render immune the animal which is to furnish the antitoxic serum.

A bouillon culture of very virulent Klebs-Loeffler bacilli is added to 2 per cent. peptonised alkaline and sterilised bouillon, in a 2-litre shallow and flat bottomed flask, so constructed as to give the maximum of surface exposure.

After the growth has commenced, each flask is connected by a lateral tube with a wash-bottle containing water, by which a con-

tinuous current of air is filtered and moistened before passing over the surface of the culture in the flasks.* The whole apparatus is placed in a chamber at 36° C. In three or four weeks the culture is sufficiently strong, and is passed through a Chamberland filter. The resultant is a clear bacillus-free solution of diphtherial toxine, the virulence of which is tested on guinea-pigs.

The next step is to accustom an animal to the action of this toxine, in other words to produce **Immunisation of the animal,** so that its blood becomes antitoxic. Since large quantities of serum must be available for the treatment of human diphtheria, a large animal—the horse—has been selected in preference to a smaller animal, such as the sheep or goat. Moreover, the horse tolerates the action of the diphtherial toxine well; it is the easiest large animal to immunise; it is easily bled; its serum is limpid, and according to Roux and Nocard, is not injurious to the human organism.

After eliminating the possibility of the presence of glanders and tuberculosis by the mallein and tuberculin tests, the animal is brought into good condition by rest and feeding. The immunising process is begun with $\frac{1}{4}$ to 1 c.c. toxine solution, which is injected hypodermically. A local œdema with a slight rise of temperature follows, and persists for a few days. In three days another $\frac{1}{2}$ or 1 c.c. is injected, and in three days more, 1 c.c.

During the next two weeks, about 15 c.c. are given altogether in six separate injections, gradually increasing, till by the end of the sixth week, the horse is receiving from 30 to 40 c.c. three times each week. In ten or twelve weeks, the horse is usually considered sufficiently immune, and the antitoxic power of its serum is tested from time to time. This is done by injecting a guinea-pig with a mixture of a definite quantity of the serum, and a definite quantity of toxine solution of known strength.

The urine is tested for albumen from time to time, to note that

* These conditions for obtaining the maximum amount of toxine exist naturally in the nasal passages, and suggest the reason why diphtheria in this region is so exceptionally fatal.

the toxine is not producing too much albuminuria, a point to which Roux appears to attach importance.

The Serum.—A sterilised canula is introduced into the jugular vein, and 5 to 15 litres of blood are allowed to flow through an india-rubber tube into sterilised bottles, which are then placed in a cool chamber, so that coagulation may take place. The serum having separated, is pipetted or siphoned into sterilised bottles, which, a small piece of camphor being added as a preservative, are then hermetically sealed.

To ascertain if the serum is aseptic after this manipulation, it is well to place one or two of the bottles in an incubator at 38° C., for forty-eight hours, by which time any micro-organismal growth will have become apparent.

The next step is to **test the antitoxic power** of the serum.

Suppose we take ten times the minimum dose of this toxine solution, which would be lethal for a guinea-pig, and call it 1; we then mix it with ·3, ·25, and ·1 c.c. of the serum we are testing, and inject one of these mixtures into each of three guinea-pigs of similar weight. If the first develops no symptoms whatever, the second a little local œdema, and the last dies, we conclude that ·3 c.c. of this serum is required to neutralise ten times the minimum lethal dose of our toxine solution.

A serum, of which ·1 c.c. neutralises ten times the minimum lethal dose of our toxine solution, is what Behring has named *normal* antitoxic serum, and 1 c.c. of this has a value which he calls an *immunisation unit.*

He says that a single dose of 500 units is required, and is usually sufficient, to cure a child; but as 500 c.c. is too much for injection to produce a practicable dose, the horse must be inoculated with toxine till it affords a serum 50 or 100 times more active than the serum called *normal.*

Behring's firm send it out in three strengths, as follows:—

No. 1, containing 600 units, is suitable at the onset of ordinary cases in children.

No. 2, containing 1000 units, is for severe cases in children.

No. 3, containing 1500 units, is for adults and very severe cases in children.

It is very essential to keep the vials containing the serum in a cool place, not to expose them to light, and to keep the bottles carefully corked or stoppered; each bottle is stated to contain one dose of the respective serum, but the bottles being all the same size, this implies that the dose is the same in all cases.

Theory of the action of antitoxic serum. — One of the difficulties in accepting this novel treatment by clinicians of experience has been that, close as is the connection between each link in the chain of bacteriological research, and precise as the deductions are by which the result has been attained, the adoption of the remedy as such is purely empirical, since its mode of action remains unknown to us.

There is no shutting the eyes to the fact that we are entirely ignorant of the chemical nature of toxines and antitoxines, and that before we can pursue this treatment rationally, we will have to understand their chemical composition. If we could isolate and identify the active principle or principles on which the value of antitoxic serum depends, with as much accuracy as we can isolate strychnine or morphine, then we would have something definite to work with. A great difficulty in attaining this is that these bodies exist in almost imponderable quantities. But the advantage of such information would be that we could employ only the beneficial principle, and reject the unnecessary and possibly noxious constituents of the complex body which we in our present ignorance call "antitoxin," and of the still more complex "antitoxic serum."

We note with satisfaction that this vitally important subject has been adopted as the first for investigation under the terms of a munificent gift by a City Company for the purpose of further research into the many problems of diphtheria which still remain unsolved; and that the work has been intrusted to Dr. Sidney Martin, to whom we are already so deeply indebted for valuable contributions to the toxicology of the disease.

If one could only aceept the theory of phagocytosis in its entirety, one would then be able to appreciate the action of the remedy as a cell stimulant, and, indeed, Metchnikoff prefers to call *antitoxins* stimulines.

On this hypothesis we can understand why such a proportionately larger dose is used for children than for adults.

Not a few praetitioners are said to have failed with this method of treatment in ehildren, believing that the announeed dose represented that suitable for an adult. But no such regulation appears to obtain with regard to administration of the serum, for we are taught that an infant or ehild of tender years can with advantage reeeive with good effect an equally large dose as would be necessary to preseribe for an adult; and often double or three times the quantity. In other words, an infant weighing twenty-five pounds is plaeed on a level, in regard to dosage, with a man of twenty-five years.

We ought to take it then that the apparent gravity of the attack rather than either the age or the weight, is to be the indication. If this is so, may we seek an explanation in the fact that the younger the ehild the greater the suseeptibility to the disease, and the less the resistanee? Consequently, if, as is suggested, the remedy acts by cell stimulation, the greater the neeessity for a large dose of the serum; or, in other words, sinee the young cell elements are so extremely sensitive to the diphtherial poison, they require to be fortified all the more strongly in order to exercise an effective resistanee.

An alternative view of the *rationale* of its mode of action is that of Klein, who holds that the toxines cireulating in the tissues of the patient are neutralised by the antitoxin, without the intervention of the biologieal faetor whieh is implied in Metchnikoff's theory.

The same authority has proposed another method of rendering the horse immune. So far as we understand, it is as follows:—

At the eommencement of the proeess, a few injeetions are made with cultures of attenuated bacilli along with their toxic products.

The animal having thus acquired a certain amount of resistance to diphtheria, large quantities of *toxine-free* bacilli are repeatedly injected subcutaneously—each injection gradually increasing in virulence.

By this method, Klein claims to have obtained serum of sufficient antitoxic power in as early as twenty-three days, whereas, Roux, whose method is practically identical with that of Behring, by more numerous injections of toxine of definite strength, has not succeeded in effecting this end under ten weeks.

In Klein's process, the amount of toxine is not definite; its strength and amount depending on the varying numbers and virulence of the bacilli introduced.

Indications for serum treatment.—The essential one is the presence of the Klebs-Loeffler bacillus, either with or without associated microbes. But when a child, attacked by diphtheria or croup, presents symptoms of broncho-pneumonia, it is in our experience, as in that of many other observers, utterly useless to employ serum, and, indeed, it does positive harm if pulmonary tuberculosis be present. In one instance of which we have knowledge an injection of serum appeared to be directly responsible for a recrudescence of spondylitis.

Dosage.—It is impossible in the present state of our knowledge to fix the dose of serum on the datum of age, as is the case with the generality of remedies. The first dose may be regulated according to the length of time which has elapsed since the onset; and later, after a bacteriological examination has been made, the question of a repetition or of an increased dose may depend on whether the bacillus is or is not accompanied by the virulence-conferring streptococcus—in other words, if the case has proved, on bacterioscopic examination, to be a severe one.

Roux's first announcement, speaking of the serum from the Pasteur Institute, was to give 20 c.c. to every patient—adult, or child above one year, so soon as admitted, and even in advance of the bacteriological diagnosis, stating that for children under one year the first dose should be as many c.c. as the child is months old.

In very severe cases, Roux states that the dose may be as much as 30 c.c. and even more, notably in those in which it has been found necessary to practise tracheotomy.

The following has been our experience, the serum employed having been that prepared at the British Institute of Preventive Medicine, and indicated in our records by the letters **B.I.P.M.** :—More than 20 c.c. has never been given as a first dose for an adult, and the average has been 15 c.c. for a child between one and five years. For a child under one year, treatment has commenced with 10 c.c.

The number of repetitions and amounts of the repeated doses have been regulated mainly by the disposition of the membrane to separate, and by its effects on the temperature, circulation, respiration, and renal secretion. We are in accordance with those who advise that there should be an interval of twenty-four hours between the first and second injections.

It appears preferable to make the first dose a fairly large one; whether the following doses, if any, are to be more or less must depend on the circumstances of each individual case. The largest total quantity which we have seen administered was to a girl of nine years, 120 c.c. in eight equal doses.

Many cases required but one dose, and seldom more than three.

To those who desire to use other preparations of serum, the following table may be useful :—

Preparation.	Dose in C.C.	Dose in Fluid Drachms.
Roux (Pasteur Institute), .	10 to 30	$2\frac{1}{2}$ to $7\frac{1}{2}$
Brit. Inst. of Prev. Medicine (B. I. P. M.), . . .	10 to 20	$2\frac{1}{2}$ to 5
Burroughs, Wellcome, and Co. (B. & W.), ...	10 to 20	$2\frac{1}{2}$ to 5
Klein, ...	6 to 10	$1\frac{1}{2}$ to $2\frac{1}{2}$
Aronson, ...	2 to 5	$\frac{1}{2}$ to $1\frac{1}{4}$
Behring (in three strengths), .	8	2

Roux's serum is not to be obtained in this country.

The syringe should be sterilised both before and after being

used; we prefer that kind called Roux's (Fig. 63), made by Arnold, but that of Burroughs and Wellcome is equally suitable (Fig. 64).

The following are the precautions to be observed during the employment of serum treatment:—

The syringe having been taken to pieces, the separated parts

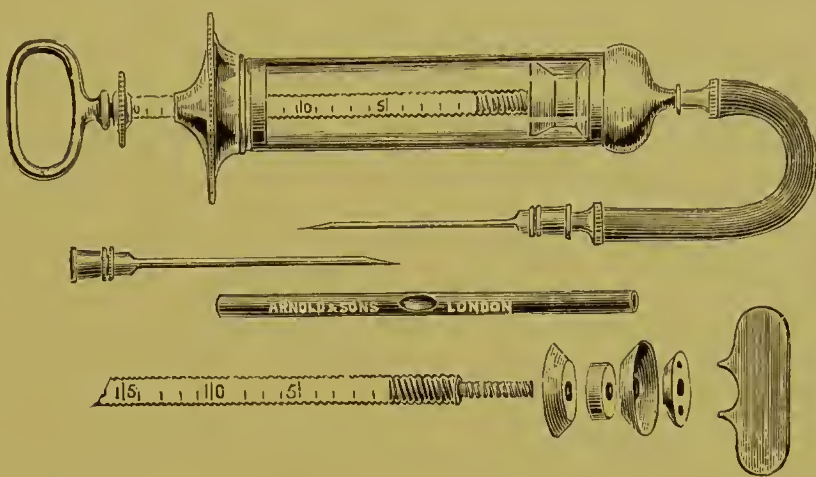

Fig. 63.—Roux's Syringe for Antitoxin, showing how each separate part can be disjointed for the purpose of disinfection.

are immersed in cold water, which should then be boiled for five minutes. They are then carefully dried. The india-rubber tube

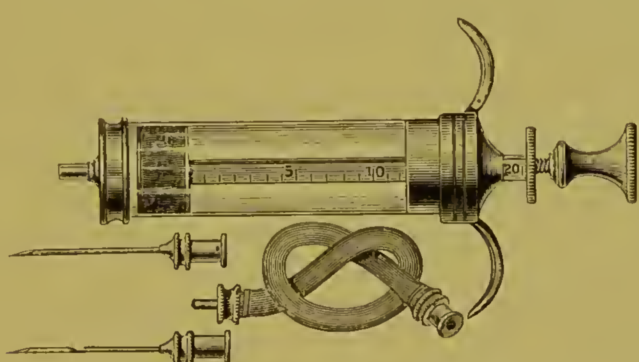

Fig. 64.—Burroughs & Wellcome's Antitoxin Syringe. also capable of easy and efficient disinfection.

is sterilised by forcing through it a stream of boiling water by aid of the syringe.

The skin is washed with an antiseptic lotion, and having selected the lower lumbar or inguinal region, the skin is pinched up by the left thumb and forefinger, the needle introduced, and the serum

injected slowly. A pad of sublimate wool is placed over the site of puncture, and, with the exuding drop of serum, forms a sort of collodion. A local œdema is produced, which usually disappears within an hour.

Results.—Many claims have been made as to the advantages of the so-called antitoxin or serum treatment of diphtheria over the former methods, but no comparative statistics have hitherto been furnished beyond those of mortality. These we now propose to supply by figures derived and classified from a series of 100 cases treated by the serum, as noted in the wards of a metropolitan fever hospital in the first four months of the present year, having taken advantage of the facilities afforded by the Metropolitan Asylums' Board to follow the course and treatment of this and other infectious diseases in the wards of their excellently administered hospitals. These results will be compared with the figures of another series of 100 cases, treated without the serum, in the same hospital at a corresponding period in the previous year, and therefore under exactly similar circumstances of situation, season, administration, and hygiene. This series of results under former methods is a somewhat detailed *resumé* of a portion of the published statistics for the year 1894.

We have not failed to recognise the objections which may be made, and quite legitimately, against this comparative method of reviewing the subject. The first and most important one, viz., the absence of bacteriological diagnosis in the series of cases treated without serum, may be met by the reply that this circumstance has not been held to reflect adversely on comparisons made in favour of the new treatment; and also by the well-ascertained fact that, in the institution in which these cases have been observed, the proportion of errors in the clinical diagnosis corrected by bacteriological methods has been so extremely small (less than 5 per cent.) that the discrepancy may be almost discounted. Other objections and possible sources of fallacy will be met as they occur on consideration of the various headings to be now discussed.

The points thus offered for comparison will be found to touch on almost every particular that has been advanced in favour of serum treatment :—

1. The mortality, actual, and as calculated for age periods.
2. The mortality after deducting cases fatal within twenty-four hours of admission.
3. The day of the disease on which treatment was commenced.
4. The prolongation of life in cases with fatal results.
5. The site of the membrane.
6. The day of treatment on which the membrane commenced to separate.
7. The day on which the throat was declared free of membrane. Under this heading will be subordinately considered the disposition for membrane to extend, and to re-appear.
8. The temperature.
9. The pulse.
10. Skin eruptions and joint pains.
11. Adenitis.
12. Otorrhœa.
13. Renal complications :—

    (*a.*) Albumen; (*b.*) Urea; (*c.*) Phosphaturia; (*d.*) Anuria; (*e.*) Nephritis.

14. Cardiac failure.
15. Other causes of death.
16. Paralytic sequelæ.
17. General well-being during treatment and convalescence.

The serum employed was in all cases that provided by the British Institute of Preventive Medicine.

Series "A" refers to cases under former treatment, and Series "B" to those under serum treatment.

The latter comprises 61 completed cases, the first treated on January 2nd, 1895, and 39 who were still in hospital on April 30th—the last day of our observation—none of them having been admitted later than April 8th.

According to seasonal mortality curves, the first three months of the year may be taken to represent a period of average fatality, and in the opinion of the Medical Superintendent of the hospital under observation, the disease, as witnessed in the early part of the present year, differed from the average rather on the side of increased mildness (*Lancet*, Feb. 2, 1895).

The following division of our 1000 cases, in which there were 284 deaths, into separate hundreds, shows how uncertain these variations of mortality are :—

1st hundred.	2nd.	3rd.	4th.	5th.	6th.	7th.	8th.	9th.	10th.
30	27	26	36	32	37	20	30	24	22

1. **The actual mortality** in both series now under comparison was the same, namely 27. It was 27·10 on the whole number —1163—treated during the year 1894 at the hospital whence our comparisons were made.

This fact, that the mortality in those under classical treatment represents the exact proportion observed in the total for the year 1894, shows that the series may be accepted as in every respect a fair standard for comparison with that under serum.

On this point of mortality it is of course all-important to select as a basis of comparison, not the results at institutions of which examples may be found in any of the Continental cities, where the former mortality has ranged between 40 and 60 per cent., but the returns of hospitals which have shown the best results under former treatment. To reduce a mortality, as in the case of Roux's Parisian statistics from 51·7 to 24·5, or of those of Budapesth under Bokai from 60·23 to 25·83, must carry a different impression to the physicians of the hospital where such cases are treated than it will to those who have been accustomed by long experience to a mortality of 26 or 27 per cent., as is recorded of one or two of our metropolitan isolation hospitals.

London, indeed, is not free from these discrepancies, for in these hospitals, all under equal conditions of administration, a difference in death rate may from year to year be observed to the extent of 13 or 14 per cent. In other words, the mortality in the hospital with the highest death rate can be seen to be half as high again as that in the hospital in which it is lowest; nor can this difference in results be due to variations in type of the disease in any one particular metropolitan district, because it is well known that patients are admitted into our fever hospitals, not according to district but according to accommodation, a return of which is daily made to the central office.

Mortality at age periods.

One of the strongest claims advanced in favour of serum treatment has been that infant mortality has been markedly decreased under its use, but the following figures illustrate that so far as age was concerned, while the number of cases under five was considerably in excess in Series "A," the mortality was less by over 10 per cent. On the other hand, there is an improvement in the results at the more advanced age periods in Series "B."

Age.	Series "A"—27 deaths. Number of Cases.	Series "A" Number of Deaths.	Series "A" Mortality per cent.	Series "B"—27 deaths. Number of Cases.	Series "B" Number of Deaths.	Series "B" Mortality per cent.
Under 5	51	22	43·1	43	23	53·48
5 to 10	28	3	10·7	37	3	8·1
Over 10	21	2	9·5	20	1	5·0
	Five cases were over 21 years of age, ranging from 22 to 36.			Eight cases ranged from 21 to 39.		

Under former methods, no deduction can be made for *withheld treatment* in the case of patients admitted moribund or declared beyond hope, a circumstance which has undoubtedly obtained in many hospitals where serum treatment has been pursued on a large scale, and naturally to the advantage of their statistics.

If, however, allowance were to be made in both instances for cases which have proved fatal within twenty-four hours after admission, as has been very generally urged by all advocates of serum treatment, the result would not, according to our figures, be in favour of serum.

2. Mortality after deducting cases fatal within twenty-four hours of admission.

	Series "A."		Series "B."	
Age.	Deaths within twenty-four hours.	Reduced Mortality.	Deaths within twenty-four hours.	Reduced Mortality.
Under 5	10	21·5	3	46·5
5 to 10	1	7·1	0	8·1
Over 10	0	9·5	0	5·0

At the hospital from which these figures were taken, 1249 cases of diphtheria were treated in 1893, with a total mortality of 332, or 26·4 per cent. Had allowance been made for 49 cases which died within 24 hours of admission, this mortality would have been reduced to 283, otherwise to 22·6 per cent.

The total mortality for 1894 in this same hospital was 314 out of 1163 cases treated, or 27·10 per cent. With similar allowance, the mortality would be reduced by 41 cases, in other words to 23·4 per cent.

3. The day of the disease on which treatment was commenced.

A claim has been strongly urged for commencing the serum injections at the earliest possible moment, and elaborate figures have been prepared, showing the increased mortality in proportion to the delay in its adoption. But such a proviso should surely apply not only to diphtheria and to a particular treatment, but to every disease and to all therapeutic measures.

In hospitals for diphtheria, where it is the rule for nurses who have the least symptom of sore throat to present themselves to the medical superintendent for immediate examination, and where

the disease is, therefore, attacked at once, a fatal result is almost unknown, and this under the former methods of treatment. In the hospital in which these observations were made, 42 cases of diphtheria have occurred in the staff during the last five years, without a single fatal result.

The following figures show that there is no warrant for special application of the general law that the earlier the treatment the better the result, since the day of admission was practically equal in both series :—

Day of Commencement of Treatment.	Series " A." Number of Cases.	Series " B." Number of Cases.
1	2	2
2	29	24
3	22	32
4	20	17
5	8	9
Over 5	19	16

4. The following figures show the **prolongation of life in cases with fatal results** :—

Day of Death.	Number of Deaths.	
	Series " A."	Series " B."
Within 24 hours, ...	11	3
2nd day, ...	2	1
3rd "	4	3
4th "	3	4
5th "	1	2
6th "	3	1
7th "	1	1
8th "	1	4
9th "	0	1
10th "	1	0
16th "	0	1
21st "	0	1
32nd "	0	1
38th "	0	1

The average length of time before the fatal termination was 3·3 days in Series " A," whereas in Series " B " it was 8·79.

This prolongation of life has been claimed as an advantage of serum, and without doubt, as a general rule, it implies an increased chance of recovery; but in the case under consideration it is capable of a contrary interpretation, for it would appear to indicate the acquirement of something in the system which entails a longer time for full elimination of the toxin of the disease, with a consequent diminution of recuperative energy, and final failure. Thus, while in all serum cases there is a tendency for convalescence to be delayed, in those terminating fatally, death is simply procrastinated, and the period of suffering of the patient and of anxiety to the parents is unduly extended.

5. **The site of membrane** is to be considered as an important indication of the relative gravity of the two series of cases, and although Series "A" has fewer examples of nasal diphtheria—the most fatal form—*per contra*, it has many more examples in which the membrane extended to the larynx, and a larger number of tracheotomies.

Site of Membrane.	Series "A."	Series "B."
Fauces, ...	60	65
Larynx, ...	2	0
Fauces and Larynx, ...	16	3
Faucial and Nasal, ...	17	28
Faucial, Nasal, and Laryngeal, .	1	2
Nasal, ...	1	1
Hard Palate, ...	0	1
Faucial and Palatal, ...	1	0
Faucial and Buccal, ...	1	0
Faucial and Vulval, ...	1	0

With regard to *nasal* diphtheria, whether in association with the fauces or larynx, or both, we have found in 1000 cases, tabulated with regard to site and other items of interest, that this variety was fatal in 67 per cent.; and in the present comparison we find in Series "B" a total of 31 cases of this class, 16 of which ended fatally—in other words, 50·16 per cent. This is in favour of the serum, for under the older method of treatment, as repre-

sented in Series "A," out of a total of 19 cases, 12 died—or 63·15 per cent.

In the cases in which the *larynx* was involved, in Series "A," 7 died without operation, out of a total of 18; these included one case which died within twenty-fours of entrance to the hospital, intubation having been performed previous to admission; 4 tracheotomies were performed, of which number 2 died.

In Series "B" there were 5 cases of laryngeal diphtheria, and of these 2 died; in one of the fatal cases tracheotomy was performed. These numbers are certainly too small to deal with, but evidence from other sources is distinctly in favour of serum treatment with regard to laryngeal diphtheria.

6. The day of treatment on which the membrane commenced to separate.

According to Roux and many other observers, the **false membranes** cease to spread at the end of twenty-four hours, commence to be detached twenty-four hours later, and do not persist more than four or five days. The early experience of English observers—ourselves amongst the number—tended to agreement with these statements. The membrane was generally reported to early undergo a whitening process, a fissuring of its surface resembling the "crackle" marks on old china, and a notable eversion of the edges. When it separated there appeared to be certainly less bleeding from the underlying tissue, and less hæmorrhage was observed to follow assistance in removal of semi-detached portions. Evidence was given that the membranes, when separated, showed little disposition to re-deposit.

When, however, these articles of assertion and belief come to be tested by figures, not much is really found to the advantage of serum on this point. It requires to be noted particularly that this point of speedy separation was not attended to very much under the pre-serum methods of treatment. Consequently we have only 50 cases in Series "A" from which to draw comparisons.

It is to be understood, with regard to the serum series, that

an injection was always made immediately on admission to the patient.

Day.	Series "A" (on 50 Cases).	Series "B" (100 Cases).
1, ...	10 or = 20 per cent.	1 per cent.
2, ...	13 ,, = 26 ,,	28 ,,
3, ...	18 ,, = 36 ,,	36 ,,
4, ...	7 ,, = 14 ,,	14 ,,
5, ...	2 ,, = 4 ,,	2 ,,
7, ...	0	1 ,,
12, ...	0	1 ,,

The full number of 100 is made up in Series "B" by 2 cases in which no membrane was visible, 2 in which there was further extension, and 13 in which death occurring the membrane had not cleared.

7. The day on which the throat was declared free of membrane.

In Series "A" this fact was noted in only 67 of the cases, and in 92 in Series "B." Only 1 occurred in which membrane reappeared, and that on the fourteenth day after admission; whereas in Series "B" there were 5 cases of re-appearance, 13 cases in which it never cleared entirely, and in 1 case it was observed as late as the thirty-ninth day after admission, and the forty-first day of the disease.

Day.	Series "A."	Series "B."
2. . . .	4 or = 6 per cent.	1 or = 1·08 per cent.
3. . . .	13 ,, = 20 ,,	4 ,, = 4·3 ,,
4. . . .	14 ,, = 21 ,,	9 ,, = 9·8 ,,
5. . . .	14 ,, = 21 ,,	18 ,, = 19·5 ,,
6. . . .	8 ,, = 12 ,,	18 ,, = 19·5 ,,
7. . . .	6 ,, = 9 ,,	10 ,, = 10·8 ,,
8. . . .	5 ,, = 7·4 ,,	2 ,, = 2·1 ,,
9. . . .	1 ,, = 1·5 ,,	1 ,, = 1·08 ,,
10. . . .	1 ,, = 1·5 ,,	1 ,, = 1·08 ,,
11. . . .	1 ,, = 1·5 ,,	0 ,, = —
12. . . .	—	2 ,, = 2·1 ,,
13. . . .	—	2 ,, = 2·1 ,,
14. . . .	—	2 ,, = 2·1 ,,
17. . . .	—	1 ,, = 1·08 ,,
24. . . .	—	1 ,, = 1·08 ,,
28. . . .	—	1 ,, = 1·08 ,,
39. . . .	—	1 ,, = 1·08 ,,
	67	74 + 18 as above = 92.

Roux also affirms that the **specific bacilli disappear** with the elearing off of the membrane, or in at most a few days after that event. With this our experienee does not agree, sinee in very many eases the baeilli are proved to be present for several weeks after the attaek has passed, in spite of attempts to hurry their departure by means of antiseptie gargles and mouth-washes used twiee and three times daily.

In one instanee under our observation the patient was still detained in hospital on aeeount of the eontinued presenee of baeilli as many as *one hundred and forty-six days* after all signs of membrane had disappeared.

Probably removal to a eonvaleseent hospital might effeet the desired end in sueh persistent eases, eare being taken to keep them isolated from those reeovering from other infeetious diseases.

8. As to the **temperature,** no exaet eomparisons ean, of eourse, be made, but we must again eall attention to the faet that in diphtheria the thermometer by no means ranges high, and is always low, even subnormal, after full appearanee of the membrane, that is, after the seeond or third day. We, therefore, eannot appreeiate the point made as to reduetions in the " fever " of the disease.

In no ease have we seen any notable reduetion in temperature after an injeetion of serum, as has been so frequently stated. On the eontrary, there is almost always a rise, small it may be, and often of but a few hours in duration.

We have no desire to magnify the importance of this matter of faet, but we agree with the remark of Variot that an elevation may be easily overlooked unless the thermometer be used at least every four hours. In non-diphtherial eases of membranous throat, this physieian has noted that eaeh injeetion of serum eauses a rise of temperature of from half to one degree, and sometimes more.

The temperature in pure diphtherial eases, aeeording to Louis Martin, falls after twelve hours, but had he reeorded the temperature more frequently than twiee a day, as his published eharts only show, it is not unlikely that this fall would have been notieed to

be preceded by the slight rise of temperature soon after the injection, of which it has been thought a duty to make note.

In cases in which the streptococcus is associated with the diphtheria bacillus, L. Martin notes a rapid rise of about one degree after some of the injections. An examination of his charts of complex diphtheria reveals the fact that it is the rule for the second injection to be followed by a gradual rise of temperature for twenty-four hours, whereas, in purely diphtherial cases, the second and subsequent doses are not, as a rule, followed by elevation.

9. As to the **pulse,** after a dose of serum has been administered we find the rate somewhat increased concurrently with the rise in temperature—in one instance it went up immediately from 136 to 166; and we have been unable to detect any diminution in tension, as has been claimed by some observers. In pure diphtheria of a mild type, the first dose, according to L. Martin, at once diminishes the pulse rate; but with streptococcal associations there is a very marked increase, always after the first, and sometimes after the second.

Variot has lately drawn attention to the quickening of the heart's action, cardiac asthenia, and arhythmia of the pulse, as a sequel of injection of serum.

10. Skin eruptions and joint pains constitute another element on which no comparison can be made, for in Series "A" rashes were practically, and joint pains absolutely, absent. In one case erythema nodosum was observed, and in another, a male aged thirty-five, eczema was present on admission. In Series "B," 38 of the cases developed eruptions which varied in occurrence from the seventh to the twelfth day, and were of the varieties which have been generally recorded. In several instances, when a fresh injection was made, after an interval of some days, the eruption broke out anew. In four cases there were joint pains.

Our figures are greatly in excess of those recorded by Moizard

who, out of 231 cases treated by serum, noted 33 rashes, namely, 14 of urticaria, 9 of scarlatiniform erythema, 9 of polymorphous erythema, and 1 of purpura. This physician reports that urticaria is noticed at a period varying from a few hours to as many as fifteen days after injection. It is seen more or less over the whole body, in successive crops, and unaccompanied as a rule by high temperature. The erythematous form of eruption is more severe, as it is accompanied by high temperature, and, as Moizard relates by phosphaturia. Joint pains, simulating those of acute rheumatism, are distinctly more common under serum treatment; they are rarely found along with a rash, and are less frequent than skin eruptions. We have already noted in our chapter on clinical diagnosis that rashes are not unknown in diphtheria, but under serum treatment they are decidedly more common, occur at a different stage, and also in non-diphtherial cases in which serum has been used. Besides, joint pains in pre-antitoxin days were practically unknown, except in cases of complex diphtheria of malignant type.

It has been advanced by laboratory workers that these eruptions and articular swellings are of no clinical importance. This opinion requires no refutation from a clinician; for such accidents, whether rare or frequent, mild or severe, clearly indicate a truly toxic origin.

The serum coming from certain horses has been observed to have a more marked toxic effect, due, perhaps, to the species, age, or state of health of the animal, for clearly it cannot be guaranteed that absence of glanders or tubercle exhausts the whole gamut of possible blood infections. Does this suggestion offer the explanation of a difference between 38 per cent. of such undesirable effects of the remedy in our series of 100 cases as distinguished from 14·3 per cent. in the much larger series of Moizard? Without offering a reply, it would be well to avert the possibility of such an insinuation by employing a serum more capable of being accurately tested with regard to uniformity and purity. The suggestion of Fraser and Ruffer to evaporate the serum *in vacuo*,

and to obtain the antitoxic body in a solid form, to be dissolved in water before use, is a good one. Klein, we understand, is now working with this same object in view.

11. **Adenitis** was observed in 18 cases in Series "A," and in 28 cases in Series "B."

In some instances the serum injection appeared to lead to a rapid, although sometimes only temporary, diminution in glandular enlargement where it existed on admission. The proportion of cases which went on to suppuration was about equal in the two.

In connection with this question of suppuration, we may mention that there were two cases of abscess at the site of injection. The following is an example.

A female child, aged 5 years, admitted January 10th, 1895, on the third day of her illness, which began with rigors and sore throat.

On admission.—Membrane was observed in a thick mass on the right tonsil, which was enlarged; the cervical glands on the same side being swollen and tender. *Temperature*, 98·2°; *pulse*, 100.

15 c.c. of serum (**B. I. P. M.**) were injected with the ordinary precautions under the skin of the abdomen in the lower part of the right flank.

January 13th.—Membrane entirely gone, the throat appearing quite clean. *Temperature*, 98·2°; *pulse*, 100.

February 9th.—There is a fluctuating swelling over the site of the injection about the size of a Tangerine orange, fairly circumscribed, and surrounded by a hyperæmic zone; it is very tender to touch, and painful when the child attempts to move. *Temperature*, 100° F.; *pulse*, 108.

February 10th.—Under chloroform the swelling was incised, and a quantity of thin pus was evacuated. On examination the abscess sac was found to be multiple; the whole cavity was thoroughly washed out with warm boracic solution, and a drainage tube inserted. *Temperature*, 100·2°.

February 12th.—Doing very well, though a large opening remains where the abscess formed. *Temperature*, 99°.

February 20th.—Wound healing. *Temperature* normal.

Ruffer has remarked how difficult it is to preserve the serum aseptic during the process of preparation, and to this cause we must attribute a certain proportion of the **accidents** of the treatment,

for they have occurred too generally to warrant any suggestion as to neglect of antiseptic precautions in particular cases.

12. Otorrhœa.

This is a complication of admitted occurrence in the course of diphtheria, irrespective of treatment. It was noted 13 times in Series "A," and 16 times in Series "B."

13. Renal Complications :—

(*a*) *Albuminuria.*—This also is a recognised symptom of diphtheria. It was found 38 times in Series "A," and 50 times in Series "B." There is no necessity to quote figures illustrating the varying quantity under the two methods, but it may be stated that it was developed in decidedly larger amounts in Series "B."

Both (*b*) urea, and (*c*) phosphates, have also, under serum treatment, been observed in excess of what may be called the amount normal to diphtheria.

It is a well-known fact that the albumen of even a non-medicated heterogeneous serum introduced into the economy results in albuminuria; and we have noted that this evidence of renal overwork has increased in frequency since the employment of serum. Lépine of Lyons, admitting that albuminuria supervenes just after the first injection of serum, asserts that it has no gravity and has no influence on the persistence of a diphtherial albuminuria; but, according to Roux, nephritis and albuminuria are less common than under former treatment. Moizard, physician to the Trousseau Hospital in Paris, agrees with him, saying that albuminuria is no more frequent under serum treatment than it was formerly, and believes, with Roux, that renal lesions are due rather to diphtherial toxæmia than to antitoxin. Ruffer goes even further, and in the *Medical Annual* for the current year, wishes "emphatically to state that there is not the slightest foundation for Mr. Lennox Browne's statement that the antitoxic serum does cause any suppression of urine."

But all these opinions are opposed to the results of the equally careful observations of Oertel, Ritter, Siegert, Variot, and many others, who accuse serum of directly provoking albuminuria.

It is difficult to account for these contrary opinions, the practical outcome of which is that while some authorities state that the timely administration of serum prevents renal complications, and others that albuminuria indicates renewed doses of serum, a last set, of which we declare ourselves adherents, believe that marked and increased albuminuria, especially if accompanied by diminished quantity of urine, should be accepted as contra-indicating a continuance of the injections.

(*d.*) *Anuria.*—Hansemann was the first to draw attention to the increased liability to anuria under serum treatment. We were particularly unfortunate in our own early experience in this respect, six patients out of a series of eight, and *not included in the present comparison,* dying with anuria as the most prominent symptom. In the series reported by Washbourn and Goodall, in which ten fatal cases were said to be due to cardiac failure, further information showed that in six of the ten there was partial anuria, and in one total anuria for the last fifty-three hours of life, the patient dying on the ninth day after the first injection; in one we learn that cardiac failure was secondary to convulsions, but it is not stated whether, as it is fair to presume, the convulsions were due to uræmia, or if, in this case, there was anuria, partial or total. Anuria, therefore, was evidenced in 7, if not 8 of the 10 fatal results. Our table of 1000 cases shows that this is a notable increase on the average of this occurrence as exhibited under "classical" treatment.

It has been asked, with regard to anuria and nephritis, if the serum would determine nephritis, how was it that there was not albuminuria in non-diphtheritic cases treated by this remedy (*Lancet*, Vol. II., 1894, p. 1539). But argument based on such an hypothesis is clearly illogical; no one has advanced the view that the serum will produce anuria in a patient who is not suffering from diphtheria, but only that it increases the well-

known tendency to renal complications in those intoxicated with its specific poison.

However that may be, the figures show that this complication is of less common occurrence in series "A" than in series "B," the numbers being respectively 2 and 7.

Many of these cases of suppression of urine bear out the fact that anuria often supervenes, not gradually, but almost suddenly, and therefore depends frequently on a paralysis of the renal vaso-motor system, to which parenchymatous degeneration, when it exists, is secondary. This would account for the circumstance that occasionally, when the anuria has been rapidly fatal and short in duration, the *post-mortem* appearances of the kidney, both macroscopic and microscopic, have given absolutely no evidence of morbid change.

(*c.*) *Nephritis.*—During 1893, out of a total of 2848 cases treated in all the Metropolitan Asylums' Board Hospitals, with 865 deaths, 8 cases of nephritis were reported. In Series "B," out of the 7 cases of anuria, nephritis was proved to exist *post-mortem* in all the 5 in which a necropsy was allowed, as well as in 4 other cases in which death resulted from other causes. In short, in all the 9 cases in which a necropsy has been permitted, out of the total of 27 deaths, nephritis has been revealed, and sometimes in extreme degree. The peculiar conditions were as follows: the distance between each two pyramids was diminished and the apices of the pyramids flattened; in many there were hæmorrhagic evidences while the capsule was sometimes firmly adherent. These figures are in accordance with those of Benda, pathological prosector to the Urban Hospital, Berlin, who has stated that on necropsy of 39 diphtheria patients treated by the serum only 6 were free from nephritis; 8 showed severe and 25 slighter parenchymatous inflammation.

Hansemann, in a personal letter to the author, referring to a case of a child who died of nephritis after injections of serum, says it seems to him "quite indubitable that the nephritis was the result of the large doses of serum which the child had received," and he

goes on to say that, "it is known that serum from one animal produces decomposition of the blood of another when introduced into it. This injurious influence may be all the greater, especially as we have no control as to whether the horses are thoroughly sound."

Treymann has reported a case of hæmorrhagic nephritis in a child aged three years. Behring's serum was employed in large doses, "owing to the unfavourable condition of the child in the early days of the disease. About the fifteenth day, albumen, blood, and casts appeared in the urine, and at the same time a measles-like eruption, with high temperature. Four days later there was anuria, lasting for forty-eight hours, and œdema of the eyelids. As the hæmorrhagic nephritis appeared during convalescence, and shortly after the last dose of the serum, and disappeared in an unusually short time, the author thinks that it should be attributed to the serum. Later, diphtheritic paralysis supervened in this case."

Opposed to this is a record of the same nature by Schwalbe, in which hæmorrhagic nephritis occurred in a case treated before the introduction of antitoxin. This author remarks on the rarity of the occurrence in diphtheria, as contrasted with the nephritis of scarlet fever, and justly urges "that the same caution exercised in attributing favourable results to the serum treatment should also be adopted in assigning to it harmful complications."

Our figures show a very considerable and undoubted increase in the proportion of cases of nephritis under serum treatment as compared with the old, for in our tabulated list of 1000 cases, mortality due to nephritis was calculated as at only 2·7 per cent., whereas under serum it has been proved on necropsy to be present in one-third of the cases—9 out of 27—and from the uniformity of its occurrence in all those examined, may be fairly assumed to have existed in a similar proportion to that observed by Benda in Berlin—namely, 84·6 per cent.

Our experience is quite in accord with those who believe that liability to this complication increases with the delay in ad-

ministering the serum, a period of the disease occurring at which antitoxin exercises a marked toxic effect. With regard to this particular and vitally important question, it may again be asked, can the difference of experience and opinion be accounted for by variation in the qualities of the serum employed ?

As these pages are passing through the press, the statistical report of the Metropolitan Asylums' Board for 1894 has been published, from which we learn that 84 cases of nephritis—occurring in a total 3666 cases treated, with 1035 deaths—were reported as a complication, representing a discrepancy of ·9 per cent. in 1893, as against 8 per cent. in 1894. But as the larger number includes 68 cases from one hospital out of a total of 642, while another does not show a single one out of 598, perhaps not much reliance is to be placed on these figures, and they are here given rather to enforce the desirability of a greater accuracy in recording these and other complications.

It is only fair to quote the experience of Professor Baginsky, which comes to us still later. On a comparison of 993 cases without serum and 525 with, he has come to the conclusion that the injection of serum does not increase the frequency of nephritis, giving tables in support of his contention. This observer is careful to give separate and widely differing figures for "clinical nephritis" as distinguished from that observed *post-mortem*.

14. Cardiac failure.

There was only 1 sudden death noted from Series "A" due to cardiac syncope, whereas 4 occurred in Series "B," and here it is again permissible to quote the experience of Washbourn and Goodall, who, ascribing 10 deaths to the poison of the disease out of 61 cases of true diphtheria treated by serum, afterwards reported, in response to enquiries, that all these died of cardiac failure.

In a debate on antitoxin reported early in the present year, Baginsky remarked that "he thought attention should be paid to symptoms of cardiac failure, which seemed to be disproportionately frequent in the recent epidemic, for most of those dying

under the treatment died from cardiac asthenia." But quite recently he was reported in the *Lancet* to have said at Munich that "cardiac debility was very rare, and myocarditis was seldom found by *post-mortem* examination." The professor's position would appear to be with regard to the heart—that minor degrees of disturbance are met with more often, the severer less often, with the serum treatment.

On the other hand, Rauchfuss, of St. Petersburg, is reported in the *Lancet* to have said at Munich that, "under antitoxin, myocarditis was more frequent; perhaps that might be due to the fact that a greater number of patients remained alive." It is somewhat difficult to understand how this condition could be judged to have been more frequent, except as a result of *post-mortem* examinations.

15. Of other causes of death in Series "B," 6 were due to **broncho-pneumonia**, and 1 to **septic peritonitis**. We may here revert to the very long period in which the patient's life is held in the balance in serum treatment, the scale being in the end but too frequently turned adversely.

Lastly, we must draw attention to the fact that more than one instance has been reported of deaths following an injection with more or less suddenness, which have been frankly accepted as due to the treatment, and not to the disease.

16. Paralytic sequelæ.

In our 1000 cases, and also in the 2848 treated in the Metropolitan Asylums' Board hospitals during 1893, paralyses were noted in 14 per cent. of the cases, and this is the exact number which occurred in the Series "A" and "B." The latter, however, includes 39 cases which have only been under treatment twenty-two days. In all of these the vital prognosis is favourable, but should a similar ratio of paralysis continue, the number in series "B" will exceed that in Series "A."* Baginsky remarked at Munich

* No further deaths, but several more cases of paralysis (May 25, 1895).

that "paralysis is more frequent under antitoxin than before; perhaps because more children remain alive."

If, as all are ready to admit, the serum acts most beneficially on that portion of the morbid influence which is due to the bacillus, as distinguished from those for which associated cocci are responsible, these results should be logically less frequent, rather than more so.

17. General well-being during treatment and convalescence.

Some very roseate statements have been made as to the rapid and very marked and favourable change in the complexion, expression, and vigour which results from serum treatment. These we have not observed with such uniformity, or even frequency, as to justify the circumstance being claimed as a beneficial result of serum therapy. As to the later stages of recovery, any one who has visited diphtheria wards in which the serum treatment is used, cannot but be struck with the greater increase of pallor and listlessness on the part of the little patients than was formerly observed, even after the acute stages have been passed, and the throat is clear of membrane. This is in accordance with the statement of Sanarelli, who affirms that all injections of curative serum are followed by leucocytosis, which process, however, he believes lends support to the phagocytic theory, and to be therefore beneficial.

Mya has noted the same circumstance as the most obvious physiological, albeit transitory change in the blood which follows on a serum injection. While not appearing to adopt Sanarelli's deduction, he disagrees with the suggestion of Zagari, Calabrese, and others, that this is the result of any noxious action of antitoxic serum, affirming that it is due solely to dilution of the blood caused by the injection of a heterogeneous serum, even in non-diphtherial cases. Nevertheless this globulicidal effect of serum injections has attracted the special attention of our American *confrères*, who consider that it is a point quite overlooked by the founders of the treatment, German and French

alike. Gabritchewsky and Morse, on the other hand, point out that leucocytosis is a normal phenomenon of reaction against diphtherial toxaemia.

The truth is probably to be found at the crossway of all these various statements and opinions; but whichever theory be correct, there can be but little doubt that, in respect of this as of other diphtherial process-changes, serum therapy does occasionally overshoot the mark. This we have seen to be the case in our comparative study of the clinical phenomena of the disease. It is equally to be noted during convalescence.

A greater number of children have been found liable to attacks of cyanosis and fainting, with a correspondingly increased demand for strong doses of nervine and alcoholic stimulants. Complete recovery is for the most part found to be greatly delayed, and an unexpected fatal result at a late period is more frequent.

Conclusions.

In our record of the clinical observations on this treatment, we have endeavoured impartially to reflect the experience of those Continental and home workers with whose results we are most familiar, and have recorded, with all reserve and deference, our own experience, whether it has agreed or disagreed with those conclusions. We must put it on the credit side of antitoxin that there is decided evidence outside our personal experience of diminished mortality in infant life; and also of improved statistics with regard to intubation and tracheotomy. Our own observations record an improved mortality in nasal and laryngeal diphtheria, with a diminution in deaths from mechanical obstruction.

In few of the returns has any statement been made—indeed, information on this point has even been suppressed—as to whether antitoxin was used as a substitute for all other treatment or as an adjuvant. The latter was the case in our series. The point is of importance from several aspects, both *pro* and *con.*

When drawing attention at a meeting of the Clinical Society

last December to an increased liability to the most grave complications of diphtheria, viz., anuria, nephritis, and cardiac failure under the use of serum, we took occasion to express a hope that further experience might prove that the disadvantages of serum would be more than outweighed by its benefits. We deeply regret to be obliged to record facts which, if confirmed—and they are easily capable of being checked by parallel observations of others who may elect to make use of the opportunities which we have embraced—cannot fail to carry a contrary conviction. The question is, indeed, enforced on us as demanding an early reply, whether we are justified in continuing to pursue a treatment, the efficacy of which, in December 1894, seemed, in the opinion of the Clinical Society of London, "to be assured," but in which there is such a marked increase in some of the recognised complications of diphtheria, and the occurrence of several new ones of undesirable, if not actually of fatal, significance. It may be that in some of the Continental hospitals, and even in those of our own city, where the mortality has hitherto been abnormally high, the results of serum therapy will be such as to suggest that the improvement is the direct outcome of the new remedy. But for reasons already stated, this reduced mortality may in a large measure be due to an amelioration of the *personnel*, which is the inseparable concomitant of all serum therapeutics, and by no means the least important factor in the attainment of a lowered death rate.

It is not unlikely that by a similarly increased observance of precautions against sepsis, the classical treatment will also in the future yield still better results.

If further experiment be deemed necessary, the two methods should be offered parallel chances by treating in the same institution each alternate patient by the one or other method respectively, with a careful comparison of the results.

Whether the efficacy of the new treatment be finally accepted or disproved, we shall feel that we have accomplished a plain duty in reporting the foregoing facts as they have presented themselves

during some months of close observation in an institution which has attained the premier position in regard to low mortality for some years past, by those methods of treatment known to us prior to the introduction of antitoxin.

While correcting these pages we observe that Dr. Winters, of New York, has arrived at similar conclusions to ourselves on several of the points which we have considered.

Employment of serum as a prophylactic.—The foregoing observations as to the effects of serum treatment will, we trust, have made it clear that the injection of antitoxic serum into a patient attacked by diphtheria is not altogether free from an added danger, notwithstanding that the amount of active principle administered can be measured only by millionths; and we have seen that the power of this serum to do good and *per contra* its capacity for inflicting injury is in proportion to the duration of the disease—in other words, to the degree of the toxæmia.

As a corollary, we might be able to pronounce that the power of antitoxic serum to act as a prophylactic against a possible attack of diphtheria is in proportion to the vigour and healthy blood condition of the individual in whom it is employed: but the very minute dose administered for this purpose is evidently capable of being soon broken up by cellular action in the healthy.

We can, therefore, understand the general admission as to the evanescent character of the immunity so obtained. Moreover, reports of cases are not wanting in which noxious and even fatal results have followed the use of serum when employed as a prophylactic.

On all these grounds, therefore, we do not feel justified in recommending serum for this purpose.

More real methods of preventing the spread of diphtheria are to be found in improved sanitation, in prophylactic surgical treatment already detailed, and in efficient isolation and disinfection.

INDEX OF LITERARY REFERENCES.

GENERAL INDEX.

**** As, unless otherwise stated, all details refer to "DIPHTHERIA," this word is not reiterated.*